Pandemic Perspectives

The science and politics of COVID-19

Contents

Presented by Consonant CUSTOM MEDIA

Introduction

The year 2020 will likely be studied historically as "life during the time of coronavirus." Life in 2020 has been a time of social distancing, mask wearing, mask-shaming, politics, surges in virus cases, testing, not enough testing, "super-spreader events," too many deaths, more politics, White House Coronavirus Task Force briefings that were political events rather than actual briefings, red states, blue states, and lots of "uncertainty."

A major killer

As if you needed a reminder, COVID-19 is the worst pandemic since the "Spanish Flu" of 1918 that killed an estimated 50 million worldwide. Our 21st century pandemic has been unlike any other – both in its ability to infect and kill people and also in the way governments around the globe have responded, or not responded. The United States' response has received poor grades due to the lack of a unified, "all of government" approach, a task force whose efforts have been hampered by misdirection and politicization, and an administration that has provided the opposite kind of needed leadership (unifying, steady, staying on message and modeling good behavior) to effectively face a public health crisis of these proportions.

This eBook is a compilation of blog posts written by three members of the CCM Team during the COVID-19 pandemic. We began blogging about the coronavirus in mid-March, when it began to have its first significant effects on our economy, livelihoods and lifestyles.

The politics of the pandemic

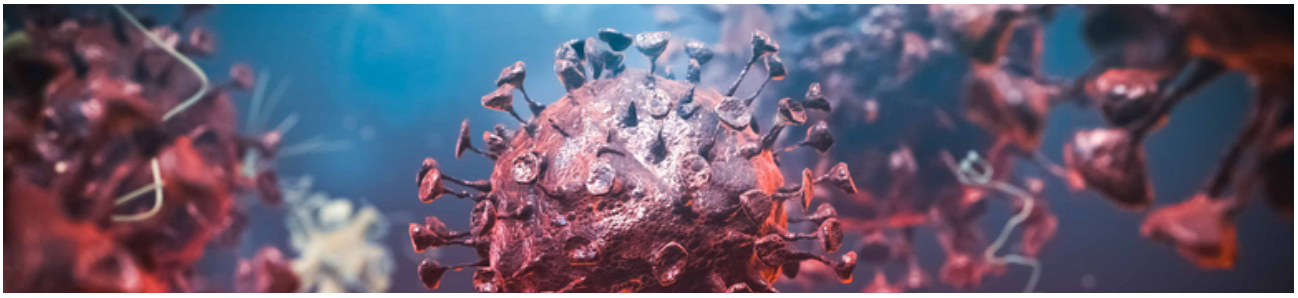
Although it has never been our intention to make either this publication or the CCM Blog political in nature, much of the public and private response to the pandemic in this country has been along political lines. This reality makes it impossible for us to ignore the politics of the pandemic.

As we finish curating the posts for this book in early November 2020, the USA is on the verge of recording its 10 millionth case. Once more, the virus has killed nearly 240,000 Americans. The "fall surge," long predicted by infectious disease experts, is well under way.

But there has been some good news. As President-Elect Joe Biden announced the members of his pandemic task force, the drug company Pfizer has announced that early analysis showed its vaccine candidate for COVID-19 is more than 90 percent effective at preventing infection. If that vaccine proves to be as effective as it appears in early clinical trials, the next big step is getting it distributed nationally and globally.

Beginning at the beginning

We have published the COVID-19 posts in chronological order. Please visit the CCM Blog to keep track as we continue to cover the pandemic.



Do our COVID-19 Hopes Rest on Remdesivir's Success?

By Randolph Fillmore
March 15, 2020

The "Swiss army knife" of viruses

On a recent National Public Radio program, Mark Denison, MD, professor of Pathology, Microbiology and Immunology at Vanderbilt University, called the corona virus sweeping the world the "Swiss army knife" of viruses.

He explained that the virus, called SARS-CoV-2, which causes a disease called "COVID-19, is a "jack-of all-trades," a unique corona virus, highly infectious, able to easily adapt, with a structure that enables it to "pick the lock" of human cells and enter. Once inside the cell, it replicates and causes havoc.

Other corona viruses, such as severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) are related corona viruses, but SARS-CoV-2 is unique, said Denison, who has studied a variety of corona viruses for over two decades, Denison added that virologists knew that something like SARS-CoV-2 would emerge eventually but did not know when. Potentially good news, he said that SARS-CoV-2 is "one type" and that it is not evolving.

Structure and function

The spikey nature of the corona on SARS-CoV-2, looking like a crown, or sharp rays coming from the sun, gives corona viruses their moniker. According to University of Texas-Austin researchers, the "tool" the virus uses to break into cells is a "spike protein" on the cell surface that binds with a receptor protein ACE2 on the surface of respiratory cells. Targeting that interplay between the spike protein and ACE2 "cracks" the cell. Disrupting that interplay might be the key to "cracking the case" of SARS-Cov-2. They published their research in the March 13, 2020 issue of *Science Magazine* (AAAS).

On his university website, Denison says that corona viruses are a genetically diverse family of viruses that infect birds and mammals, with most strains infecting only certain "hosts." Human corona viruses cause up to 30 percent of common colds. When viruses jump between animals and humans, they are referred to as "zoonotic."

In the last 15 years, explains Denison on his website, coronaviruses have demonstrated an ability to "jump into new species" and cause both SARS and MERS.

Don't be fooled into thinking that SARS-Cov2 is like the flu. It's not. Influenza is known to migrate seasonally, but the corona virus called SARS-Cov-2 doesn't need to do that. Any host, anywhere, will do. And, if it needs to, the virus can adapt. It's even been called a "proofreader" owing to its ability to adjust and correct its own genetic "mistakes" to survive.

Keep it clean

SARS-Cov2 is 1,000 times better at binding to human proteins than other viruses. However, it desperately needs a host (us) to survive. How can we defeat it? Perhaps by depriving it of hosts is one strategy, through social distancing. Speaking on a March 13 podcast from *The Journal of Clinical Oncology*, Emily Landon, MD, director of infection and control at the University of Chicago said that the "magic number" for keeping distant from anyone is six feet because that is the distance, under normal conditions, that small droplets can stay in the air. She also said that when cleaning surfaces with wipes it is necessary to observe long contact time, keeping the surfaces as wet as possible for several minutes. If you must fly, she recommended wiping down the airplane armrest, tray table, and window if you are in a window seat. If you do wear a mask you must leave it on for the whole flight. If virus is on the outside of the mask, you can infect yourself by touching it. So, be careful when removing and discarding it. Inhibiting its ability to enter cells is yet another strategy, and one being pursued.

Finding a way to keep SARS-Cov-2 from breaking into cells

It is not news that there are no specific therapeutics approved by the U.S. Food and Drug Administration (FDA) to treat people affected by SARS-CoV-2 and who have acquired the disease called "COVID-19. However, hope (springing eternal) may be on the horizon.

A re-purposed experimental drug, GS-5734, also known as "remdesivir," developed by Gilead Science, Inc. in California, mostly failed in its attempt to rescue people from Ebola a decade ago. The drug did show promise in stopping Ebola in animal models, but "fizzled" in humans, according to a March 11, 2020 article in *The Washington Post.*

The best hope is that remdesivir will rise Phoenix-like from its Ebola ashes and stop the spikey protein in SARS-CoV-2 from breaking into human cells and binding to proteins in the respiratory system, thus shutting it out and shutting it down.

As you read this, Gilead Sciences says it is working closely with many agencies, including the National Institute of Allergies and Infectious Disease (NIAID/NIH) and using it on a few patients who have contracted COVID19. Two NIH-funded clinical trials are ongoing, one at the University of Nebraska and the other is being conducted in China. Remdesivir has been called "promising."

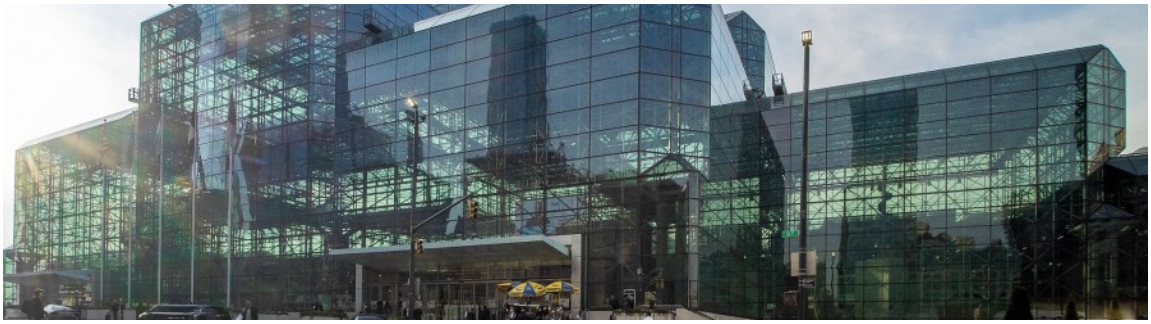
"I don't know whether it is being called promising because the company is talking about it so much, or that it is promising because it is promising," said Landon in her podcast.

Remdesivir (GS-5734) has been around for quite a while. Denison and his collaborators found years ago that GS-5734 reduced the "viral load" on the lungs of mice and improved their respiratory function.

In the past, Denison and his collaborator for almost 20 years, Dr. Ralph Baric at the University of North Carolina, in the past showed that GS-5734 could inhibit both SARS and MERS in test tube samples of human airway cells. NIAID director Anthony Fauci, MD and a member of the US Corona Virus Task Force, recently said that remdesivir has been administered to some patients with COVID-19 but that "we do not have solid data to indicate it can improve clinical outcomes."

In January 2020, Denison, Baric and their collaborators, continuing to test remdesivir in combination with other drugs, reported in Nature Communication that CoVs "…seem to play by their own rules while dancing at the edge of genetic disaster."

Let us hope that the disaster awaiting SARS-Cov-2 precedes the potential disaster looming over us. ▪



As New York's Coronavirus Cases Climb, Javits Convention Center Becomes a Hospital Complex

By Mike Eisgrau
March 26, 2020

The Jacob K. Javits Convention Center, commonly known as the Javits Center in Manhattan, is being converted to a 2,000-bed hospital complex that will be used to handle patient overflow caused by the coronavirus pandemic.

New York Governor Andrew Cuomo toured the sprawling 1.8 million-square-foot complex Monday as the Federal Emergency Management Agency works to transform the site into four, 250-bed temporary hospitals. The U.S. Army Corps of Engineers is working to construct another facility that will add a further 1,000 beds. The hospitals, each of which will cover about 40,000 square feet, will be staffed by about 320 federal medical professionals and fully equipped to handle the expected explosion of coronavirus cases.

As I write this, the NY Daily News is reporting that more than 3,700 have tested positive in New York City in the last 24 hours, raising the total in the city to more than 21,000.

After 9/11 Javits became a disaster relief center

That the Javits Center is being called into duty this way reminds me of another time when Javits and its staff stepped up to the plate. It was 9/11, almost 20 years ago.

Javits is eight minutes north of Ground Zero on Manhattan's west side. At the time I was Director of Public Affairs, chief spokesman for the Center, handling the press.

We were, at first, set up as a morgue. But when a grim reality sank in – that there were no bodies – we pivoted to become a major emergency disaster relief center, the staging area for most all you saw at Ground Zero.

We operated that way for the next five weeks, with FEMA in one of our giant halls, state and national guards in another, 500 state troopers (Javits is a New York State facility) in a third, and 5,000 volunteers.

Our giant kitchens turned out between 6,000 and 9,000 meals a day, 24/7.

One hall, a block long and completely dark with 900 cots, provided a resting place for weary workers who would come by truck from Ground Zero, fall down on the cots and get a few hours sleep. When they awoke we'd feed them and send them back down to continue their grim task.

Tony Sclafani, the guy who has my old job at the Javits, told the NY Daily News earlier this week, "Our workforce is proud to help during this unprecedented crisis. We're all in this together."

Yes Tony, we truly are all in this together. And I know you and the staff at the Javits Center – nearly two decades after 9/11 – will be up to the task.

ABOUT THE JAVITS CENTER:
The Jacob K. Javits Convention Center, commonly known as the Javits Center, is located on Eleventh Avenue, between 34th and 40th streets, New York City. It was designed by architect James Ingo Freed of Pei Cobb Freed & Partners. The space frame structure was begun in 1980, finished in 1986, and named for United States Senator Jacob Javits, who died that year. When the Center opened in 1986, it replaced the New York Coliseum as the city's major convention facility, making way for the demolition of the Coliseum and future construction of the Time Warner Center at Columbus Circle.

The Center is operated and maintained by the New York Convention Center Operating Corporation, a New York State public-benefit corporation. Home to auto shows, comic book conventions and countless trade fairs, the convention center has a total area space of 1,800,000 square feet and has 840,000 square feet of total exhibit space. It is billed as one of the busiest convention centers in the United States. ▪

EDITOR'S NOTE:
Mike Eisgrau was director of public affairs at the Javits Center from 1996 to 2005.

To N95 or Not to N95?

By Randolph Fillmore
March 27, 2020

Infection control specialist says CDC gave out impractical and misleading information on COVID-19 PPE advice.

Americans may lose faith in the U.S. Center for Disease Control (CDC) if they listen to a podcast from the Journal of Clinical Pathways on March 24. Priya Sampathkumar, MD, infectious disease specialist and hospital epidemiologist at the Rochester, Minnesota Mayo Clinic, broke down truths and misconceptions about Personal Protective Equipment (PPE), such as masks, gowns and gloves needed for healthcare providers who are treating patients with COVID-19.

According to Dr. Sampathkumar, the CDC gave out "impractical and misleading information" when they made the recommendation that all healthcare workers should don N95 masks when treating those testing positive for SARS-2 virus and/or those who are ill with the COVID-19 disease caused by that virus.

"They did it during the H1N1 flu 'out of an abundance of caution' and they did it again regarding COVID-19," she told the Journal of Clinical Pathways podcast host oncologist Chadi Nabhan, MD.

N95 masks, of which there is a great shortage now, are described on the US Food and Drug Administration's (FDA) website as "a respiratory protective device designed to achieve a very close facial fit and very efficient filtration of airborne particles. The 'N95' designation means that when subjected to careful testing, the respirator blocks at least 95 percent of very small (0.3 micron) test particles. If properly fitted, the filtration capabilities of N95 respirators exceed those of facemasks. However, even a properly fitted N95 respirator does not completely eliminate the risk of illness or death."

Sampathkumar said that N95 masks are only needed during specific, invasive procedures, such as intubations and bronchoscopies. A bronchoscopy is a procedure that lets doctors look at your lungs and air passages, and is usually performed by a pulmonologist. During bronchoscopy, a thin tube (bronchoscope) is passed through your nose or mouth, down your throat and into your lungs. The invasive nature of these procedures may result in small particles of fluid to be released into the air; different from the large particles expelled when someone coughs. Except for those procedures, a simple surgical mask will be protection enough from large, airborne droplets such as those seen when people with COVID-19 cough, she maintained. For us, an N95 or other mask is not necessary; just maintain at least six feet of distance from others.

If we had followed the CDC's advice, she said, we would have used up all of the N95 masks.

She added that her first red flag indicating this was serious came on February 9 when Delta airlines announced that it was closing flights to China through April 30.

"What did Delta know then that our government wasn't telling us?" she asked.

According to Sampathkumar, this is the way it should be: A patient with confirmed or suspected COVID-19 should be in a room alone with no mask. The health care worker goes into the room wearing gloves, a gown, and a regular surgical mask with eye protection. When the health care worker leaves the room, they should take off that PPE, dispose of it, and wash up.

"Regular masks are easy to make!" she said. "A third grader could make one." For her, the first big mistake was the U.S. government not taking supplies from the World Health Organization (WHO) and depending on CDC. "This is what happens when government agencies don't react in a timely manner." ▪

Social Distancing to Survive, Circa 1347

By Randolph Fillmore
March 23, 2020

"Bubonic plague is the inescapable reference point in any discussion of infectious diseases and their impact on society," wrote Frank M. Snowden in a recently published book looking at the history of epidemics and their impact on societies.

One inescapable reason for looking back to 14th century Europe is that "social distancing" was the only hope for curtailing spread of the Black Death, a disease that killed many, many millions. Nearly 700 years later, in an age of science, we are practicing medieval methods to try to contain COVID-19 disease. How did that strategy work then, and will it work now?

Give us some Slack


THE DEAD CART.

Back in 1988, at the height of the HIV/AIDS epidemic, Paul Slack, British historian and Oxford University professor, published a paper in Social Research (Vol 55, No. 3) on responses to Black Death and their implications for public health. According to Slack, these are some of the "social distancing" strategies Europeans used to try to curtail the spread of disease, even when the causal role of rats and fleas and the concept of contagion were not known:

- Early reactions by civic governments to outbreaks was a denial of their existence for as long as possible as they were a threat to commerce
- Plague victims were isolated, and their contacts traced and incarcerated
- There were restrictions placed on movement and quarantine regulations on travelers and shipping
- Games and festivals were banned
- Children were prevented from playing in the streets
- The infected were isolated in their houses

Slack's research showed that people who suffered the most from the plague were most often those who opposed the efforts of authorities to gain control; there was popular resistance to quarantines. The result was the initiation of "medical police." Because there were no scientific explanations, the Christian view of the plague included its supernatural origins. There was also "scapegoating," as many believed the plague was caused by Jews poisoning the water supplies.

Quarantine norms

How rigid was isolation? asked Slack. His research showed that in England the practice was total household incarceration. In the Netherlands, a more human practice allowed visits from clergymen or especially appointed "comforters." Overall, there was consensus that sacrifices need to be made for the public good, regardless of personal liberties. Slack reported that Edmund Gibson, bishop of London, said that "Where disease is desperate, the remedy must be so too."

British writer Daniel Defoe (author of Robinson Crusoe, starring a character who was no stranger to social distancing) wrote in his Journal of the Plague Year (1665), that he (Defoe) sympathized with both sides, meaning those who resisted quarantine and those authorities imposing it, saying, "There was no remedy."

Slack concluded his paper opining that "reactions to threats to public health are never purely scientific…they always involve restrictions on civil liberties of a more or less severe kind." He adds, however, that "screenings of certain groups in the population must have a clearly identified purpose."

Writing in the era of AIDS, Slack also warned that prejudice and stigma are in danger of operating… and should be kept as small as possible.

Laurie Garrett, a 21st century street corner Cassandra?

In Greek mythology, Cassandra was a daughter of Priam, the King of Troy. Struck by her beauty, Apollo provided her with the gift of prophecy. But when Cassandra refused Apollo's romantic advances, he placed a curse on her ensuring that nobody would believe her warnings. Cassandra was left with the knowledge of future events, but she could neither alter these events nor could she convince others of the validity of her predictions. (Thanks Wikipedia).

Fast forward to March 2020, 32 years beyond 1988 and almost 700 years beyond the Black Death. Laurie Garrett, Pulitzer Prize-winning public health expert and author of many books, including the best-selling 1994 "The Coming Plague: Newly Emerging Diseases in a World Out of Balance," guested on WBUR (Boston University National Public Radio) radio on March 17. Like a 21st century Edmund Gibson, she emphasized the need for social distancing in the face of spreading COVID-19 disease. And, like a 21stcentury Cassandra, she had a prediction.

What should we be doing? she was asked.

"We don't have time for the whole list," Garrett told her interviewer. "But the bottom line is that there's a role for the federal government. There's a role for the states. There's a role for local. We have this strange hodgepodge system of public health in America that is unlike any other country. And, as a result, the real burden at the federal level is a combination of setting guidances, providing sort of wise strategic policy analysis, corralling resources in a timely fashion, pushing connections between public and private sector. All should be coming together with science-based leadership from the top. And we don't have that on any single factor."

And, on social distancing? "My goodness. If people still don't understand that they need to have social distancing, then I don't think we have any hope at all. I think we're all going to drop dead," she predicted. Her calls for attention and action in 1994 were largely unheeded. ▪

SARS-Cov2 Virus and COVID-19 Disease: Made by Nature or Humans?

By Randolph Fillmore
March 31, 2020

There is a subtext to the COVID-19 pandemic that is not making it to mainstream news. It's a discussion over whether the virus could be a genetically modified Severe Acute Respiratory Syndrome (SARS) virus, manufactured through human hands. Is the virus an experiment that "escaped" from a lab? Was it released by accident? Purposely weaponized? A natural emergence? To weigh these possibilities, it is important to look at where we are with genetic engineering by human hands and intellect, especially through the gene editing technology known as "CRISPR," or other technology. It is also necessary to hear the voices that say this is a new, but wholly natural SARS virus, with no traces of human engineering.

Where to start?

Some may consider the idea that COVID-19 was manufactured and weaponized a "conspiracy theory." First, a little "weed pulling." There is no such thing as a conspiracy "theory." Problem # 1, the media and general public don't recognize the difference between theory and hypothesis.

In science, a hypothesis is a generalized idea, a guess, about what might be going on in any phenomena. A theory is a statement of fact that emerges when hypotheses are tested many times over and found to be valid. So, any notion that COVID-19 was made by humans and released as a weapon is a "conspiracy hypothesis," not a theory.

That there was more than one gunman involved in the assassination of President Kennedy is a hypothesis. It has been tested but, for the lack of valid evidence the results have not led to a second gunman "theory." Another hypothesis, and a popular one, is that aliens from outer space came to earth in the distant past to teach our ancients important things about science and engineering. It is a hypothesis that, for lack of evidence through testing, has not and will probably never rise to the level of being a theory (except perhaps to some viewers of the History Channel).

Examples of theories are Newton's well-tested ideas about gravity (easy to test) and Darwin's concept of natural selection, a theory, which is successfully underpinning modern biology and is clearly evident every time bacteria becomes drug resistant. A theory is not a weak idea, it is established fact. Theories can, however, be overturned when new hypotheses with new variables are well tested, verified and found to be valid.

The hypothesis that SARS-Cov2 was created by human hands using gene modification tools

"Genetic engineering" is advanced technology that can be a valuable tool in medicine to alter the genetic

makeup of plants and animals. Genetic engineering, genetic modification or genetic manipulation, is the direct manipulation of an organism's genes using biotechnology, which is a set of technologies. Biotechnology can be used to change the genetic makeup of cells, including the transfer of genes within and across species boundaries to produce improved or new organisms. New DNA is obtained by either isolating and copying the genetic material of interest using recombinant DNA methods, or by artificially synthesizing DNA that contains genetic information.

Gene editing is a type of genetic engineering in which DNA is inserted, deleted, modified or replaced in the genome of a living organism. Unlike early genetic engineering techniques that randomly insert genetic material into a host genome, genome editing targets the insertions to site specific locations.

One such gene 'editing" technology is "clusters of regularly interspaced short palindromic repeats," CRISPR for short. CRISPR allows the cell's genetic material to be cut at a desired location, allowing existing genes to be removed and/or new ones added.

There is speculation that SARS-Cov2 and resulting COVID-19 disease originated with biotechnological efforts to manipulate a strain of SARS (corona) virus and accidentally, or purposely, gave us COVID-19. The argument goes that the virus resulting from these efforts was either released from labs by accident, or that the creation and release of the new virus was weaponized and intentionally released. The structure of today's SARS virus is different from other SARS viruses in that it is more contagious and more easily attached to human proteins and breaks into cells more easily with its "spike proteins," the little growths that look like golf tees rooted in a golf ball. These differences have raised suspicions.

A virologist in Taiwan is a believer

Professor Fang Cho-tai from the National Taiwan University's College of Public Health stated that the research laboratory of the Wuhan Institute of Virology houses many deadly viruses for study. Among them is a SARS virus once active in Asia. At a recent conference, he said that the SARS strain causing COVID-19 is 96 % similar to the bat virus RaRG13, a virus he says is kept in the Wuhan lab. He added that the virus had to be 99% similar to be considered the same. Fang also said that French scientists said the key difference between SARS-Cov2 and RaTG13 is four additional amino acids (proteins) in SARS-Cov2. He suggested that these additional amino acids make the virus more contagious and that these additions are unlikely "natural," but were theoretically possible through some gene-modifying biotechnology application.

However, a Taiwanese American professor, Chin Lin, said at the same conference that the four additional amino acids in SARS-Cov2 are not unusual and noted that the idea that the United States created the virus was "propaganda."

What is the scientific argument against the human-made SARS/COVID-19 hypothesis?

In the National Institutes of Health (NIH) director's blog published on March 26, Francis Collins, one of the scientists who cracked the human genome some years back, debunked the weaponized, human-made virus hypothesis by citing research carried out by Kristian Andersen, of Scripps Research Institute, La Jolla, California and Robert Garry, of Tulane University School of Medicine in New Orleans and published in the journal Nature Medicine on March 17. His comment was that the researchers said this provides "strong evidence that the new virus was not the product of purposeful manipulation in a lab. In fact, any bio-engineer trying to design a coronavirus that threatened human health probably would never have chosen this particular conformation for a spike protein."

It is interesting and useful to read the comments added at the bottom of the director's blog. Unfortunately, we do not know the credentials of those who disagree with Collins and the research he cites.

The Society for Risk Analysis

The Society for Risk Analysis publishes a risk analysis guide adaptable to infectious disease events and it is relevant for analyzing COVID-19 to help determine whether the outbreak was natural or man-made. The analysis chart, called the Grunow-Finke Assessment Tool, lists 11 criteria that can be applied to any biological outbreak. The 11 criteria are "weighted," and a score needs to be over 30 points of a possible 60 to suggest terrorism. For convenience sake, each of the 11 is worth six points.

The GFT list of 11 criteria for determining if an outbreak is of unnatural origin is below. The criteria are as follows. Each criterion that could(based on what we have seen) apply to COVID-19 appears in **bold type.**

1. Existence of a biological risk: The presence of a political or terrorist environment from which a biological attack could originate.

2. Unusual strain: In unnatural outbreaks, the strains may be atypical, rare, antiquated, new emerging, with mutations or different origins, genetically edited created by synthetic biotechnology. It may demonstrate increased virulence, unusual environmental sustainability, resistance to prophylactic and therapeutic measures, or difficulty in detection and identification.

3. Special aspects of the biological agent: It cannot be ruled out that a biological agent has been genetically manipulated.

4. Peculiarities of the geographic distribution of disease: It would be unusual from an epidemiological perspective if the disease is identified in a specific region, either for the first time ever, or again, after a long period of time.

5. High concentration of the biological agent in the environment: If a biological agent is released artificially, we can expect to find it in unusually high concentrations in the air, soil and drinking or surface water over a large area.

6. Peculiarities of the intensity and dynamics of the epidemic: Characterized by the percentage of cases of a disease per unit of time or the total number of cases.

7. Peculiarities of the transmission mode of the biological agent: In general, natural epidemics will feature paths of transmission which are typical for the pathogen and its natural hosts, deviations from the natural paths of infection could indicate that biological agents have been deliberately disseminated.

8. Peculiarities of the time of the epidemic: Epidemics of certain infectious diseases occur in increased numbers during certain seasons, either because they are dependent on the weather, or they occur after certain intervals in time.

9. Unusually rapid spread of the epidemic: The speed at which some epidemics spread is determined by the virulence, resistance and concentration of the pathogen, the contagiousness of the disease and the intensity of the transmission process, on the one hand, and on the susceptibility and disposition of the exposed population on the other.

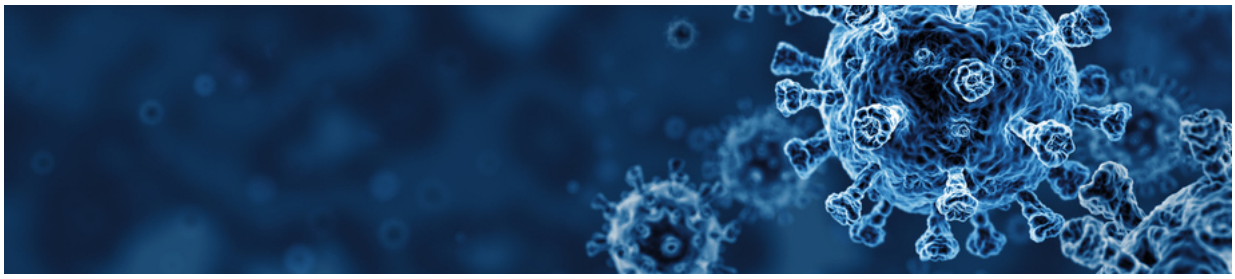
10. Limitation of the epidemic to a specific population: Biological attacks can be directed against large heterogeneous population groups and military contingents or against selected target groups.

11. Special insights: Any suspicious circumstances identified prior to the outbreak, during the period of outbreak or post-outbreak, which would point to an unnatural outbreak.

Of the 11 criteria, only four seem to fit: 4x6=24. A score above 30 might make the outbreak look suspicious.

Conclusion

It may never be determined whether the COVID-19 pandemic was caused by a natural or human-made corona virus. At this point in the pandemic's history all efforts are being made to help stop the virus from spreading and to help those who are sick or dying from it. History and future research will likely expose one truth or another truth; what is important now is to gather facts – real facts, not alternative facts – as to its origins. ▪



Clinical Trials – And Errors?

By Randolph Fillmore
April 9, 2020

Around the world, clinical trials are getting underway to find a drug, or drugs – any drugs – that will act as a vaccine for preventing COVID-19, effectively treat its symptoms or, optimally, kill the virus in people who have tested positive for it so that the disease will not progress. Most of the new clinical trials are either for remdesivir, the drug developed to treat Ebola but was disappointing in its application, or hydroxychloroquine, a drug developed and used to treat the symptoms of malaria but has also been found to be effective in treating the symptoms of both rheumatoid arthritis and Lupus, a long-term disease causing inflammation and pain. Both are non-viral, autoimmune diseases caused by the body's immune system attacking healthy tissue.

Neither drug has seen widespread, scientific testing or used in connection with SARS-Coronavirus-2, the new virus causing COVID-19, and spreading death and misery worldwide for months. With the hope that either or both might be effective treatments, clinical trials are getting underway in the US and elsewhere.

What is a clinical trial?

A clinical trial begins with a protocol, or a plan of study. The protocol lays out the research questions of interest regarding dose, length of treatment, adverse events, potential risks and benefits and who is eligible to be recruited onto the trial. The clinical trials getting underway or being planned for COVID-19 are not "normal" in that they are "interventional" rather than purely "investigational." The recognition that this is a health emergency has led to bending, if not breaking, many of the clinical trials rules, especially those regarding normal "phases" through which clinical trials are conducted.

Being enrolled in a clinical trial does not mean that you will receive the drug under investigation. Many trials include a placebo, a "fake" medication that may look like the investigational drug. Investigators need a clear picture showing if the real drug under investigation is effective, so the investigational drug is given to one group and its effects are compared to the effects of a placebo (if any) given to a group on another "arm" of the study. Some studies, especially in Phase 3, may also use another drug for comparison to the study drug, or a combination of drugs on different arms of the study. Some may use a placebo, or the test drug compared to the "standard" or previous treatment(s). The outcomes of a traditional clinical study are aimed at providing benefits to future patients, and not necessarily to benefit those enrolled in the study.

Trials using a placebo or combinations of drugs are generally "blinded" so that neither the patient nor the investigators know who is getting the drug or the placebo. Once the study is completed and "unblinded," it becomes clear what was effective and what was not. In an interventional study, investigators may still use a placebo "arm" for the study, but the beneficial results (if any) of the test drug, alone or in combination with other drugs, needs to be known as soon as possible, so an interventional clinical trial changes many things about a traditional investigational trial, especially the phases through which a study progresses and the use of other "arms" besides the investigational drug arm.

Clinical trials terminology and requirements

As mentioned earlier, a "protocol" is a plan for conducting the study in terms of which patients are eligible to be enrolled, optimal dosages of the drugs being used, including placebo, "blinding" so that patients and medical personnel don't know who is getting which drug, and randomization of volunteers to the study's various "arms" that may include placebo, no treatment, or other drugs. Volunteers must sign an "informed consent" spelling out the risks associated with taking an experimental drug. The consent form, as well as the study itself, must receive the OK from an Institutional Review Board (IRB) composed of physicians, scientists, other health care workers, perhaps social workers, members of the clergy and private citizens. The IRB protects the welfare of study volunteers. The US government requires an IRB and the IRB and researchers must adhere to US regulations from the Office of Human Research Protections under the Code of Federal Regulations 45,46. FDA regulations (21CFR) apply to any investigation of a drug or medical device. For a trial to move forward, the protocol and informed consent must be approved by a local IRB.

Phases 1-4

Normally, clinical trials go through a four-phase structural process. Phase 1 is carried out with a small group of people, perhaps more than 20 but fewer than 100, who are healthy volunteers. The aim is to determine an investigative drug's safety and tolerable dose levels without incurring adverse effects. A phase 2 study tests a larger group, perhaps from 100 to 300 volunteers, to further evaluate potential side effects and safety. In a phase 3 trial a larger group, perhaps several thousand people with the disease or condition the test drug is meant to treat, are enrolled to further evaluate the drug. A phase 3 trial will likely compare the investigational treatment against a "standard" treatment, perhaps use a placebo, or use the investigational drug in combination with other drugs. Volunteer patients are randomized to different "arms" of the study regarding which treatment they receive. These trials are usually blinded and include several "control groups" who might receive a placebo, no treatment, a combination treatment, or treatment with the investigational therapy alone. Many large Phase 3 trials will be conducted at multiple sites. The data from a Phase 3 trial will be presented to a health authority, such as the US Food and Drug Administration (FDA), or in Europe the European Medicines Agency (EMA), for approval or non-approval. A phase 4 trial is a post-marketing trial carried out after a drug is approved and has been on the market; data continues to be gathered on patients using the drug in the longer term.

The time frame for a tradition clinical trial can be from one to several years.

Interventional clinical trials to test potential COVID-19-related drugs

In normal times, a long Phase 3 trial would be necessary for testing a new drug. But these are not normal times. Today, the disease in question and the virus that causes the disease is new, or "novel," and many of the drugs being tested are being "repurposed" from treating other diseases. In some ways, the clinical trials process is being altered and might subsequently look more like a "crap shoot," Vegas-style, rather than science. But these are desperate times, and time for desperate measures.

Below is a sampling of some clinical trials around the US that are either underway and recruiting volunteers, or not being conducted yet but will start recruiting soon. They all appear on www.clinicaltrials.gov and have an identification number.

Currently, the hot trials are on hydroxychloroquine (for malaria, rheumatoid arthritis and Lupus), remdesivir (for Ebola), and trials to determine if those who have survived COVID-19 have antibodies (immunity) in their blood plasma that could be made into a vaccine to help others who may get infected to survive infection, or suffer less serious symptoms.

Selected COVID-19 trials underway in the United States

Hydroxychloroquine for those with COVID-19 and hospitalized with symptoms

A trial recently started and recruiting volunteers is a Massachusetts General Hospital/ National Heart, Lung and Blood Institute (NHLBI) collaboration for testing hydroxychloroquine among inpatients with symptomatic COVID-19 disease. It has an identifier NCT04332991 and can be found on the www.clinicaltrials.gov website. It is a Phase 3, multicenter, blinded, placebo-controlled, randomized trial with hospitalized adults. Patients on the drug arm will initially receive 400 mg of drug twice a day on the day of enrollment, then drop to 200 mg twice a day for the next four or five days. The point is to compare the drug to placebo outcomes at day 15 of treatment. The estimated enrollment is 510. The study started on April 2 and will run until July 2021. Contact 617-726-4777 or 617-724-9836 for the study nurses. The study is a multicenter study going on at 44 locations around the country. Participants must already be hospitalized.

Hydroxychloroquine to prevent symptoms in those exposed to the virus

The University of Minnesota, in collaboration with several Canadian universities, is conducting a trial to see if the study drug can prevent COVID-19 or prevent its progression in people with early symptoms. There is a treatment arm and a placebo arm. The trial started March 17 and will run until May 12. Its clinicaltrials.gov identifier is NTC04308668. Those eligible must be over age 18 and be within their first four days of symptoms. The endpoints are symptoms after 14 days of treatment. Those with retinal eye disease, chronic kidney disease, or receiving dialysis, or those taking a number of drugs (see study on https://www.clinicaltrials.gov are not eligible. Those living anywhere in the US are eligible, as are Canadians living in Quebec, Manitoba or Alberta. The study is still recruiting and expects a total of 3,000 participants. No in-person visits are necessary. For questions email covid19@umn.edu.

Study to prevent COVID-19 infection in health care workers

In Texas, **Baylor University** is currently recruiting for a trial studying the efficacy of hydroxychloroquine in preventing infection in health care workers who are at high risk for acquiring COVID-19 from treating infected patients. Estimated enrollment is 300 participants. The study, which started on April 3 and ends July 30, is not randomized. Participants will receive 400 mg twice a day on day 1, and then receive 200 mg twice a day for seven weeks. Rate of COVID-19 conversion will be tested through nasal sampling. Outcomes will look at the first clinical worsening in seven weeks. Participants must be between 18 and 75 years of age and healthy volunteers are accepted. See ID # NCT04333225 on www.clinicaltrials.gov for exclusions. Contacts are 214-820-7224 and 214-820-7965 at the Baylor University Medical Center.

Selected COVID-19 trials not yet started

The University of Utah and Intermountain Health Care will be collaborating on a study comparing hydroxychloroquine alone to azithromycin alone in hospitalized patients with suspected or confirmed COVID-19. It will be a Phase 2 study with up to 300 participants. It is scheduled to start soon and end on December 31, 2021. The clinicaltrials.gov ID# is NCT043289832.

The University of Pennsylvania will soon be recruiting for a clinical trial to prevent and treat COVID-19 using hydroxychloroquine (HCQ). The clinicaltrials.gov ID# is NCT04329923. There will be three cohorts. Cohort 1 will participate in a double-blind, placebo-controlled, high dose trial of HCQ as a treatment for home-bound, COVID-19 positive patients. Cohort2 will be in a randomized study using different doses of HCQ in hospitalized patients. Cohort 3 will participate in a double-blind, placebo-controlled trial of low dose HCQ as a preventive medicine for health care workers. A total of 400 participants is expected. The estimated completion date is December 1, 2021. Participants must be 18 years of age or older and healthy volunteers are accepted, but all must have access to a cell phone, tablet, or laptop computer with Internet accessibility. There will be

sub-studies, each with slightly different inclusion/exclusion criteria (see www.clinicaltrials.gov for details). Contact for questions is 215-509-5690.

Duke University (North Carolina) will be starting a clinical trial using hydroxychloroquine (HCQ) to determine its safety and validity for healthcare workers exposed to COVID-19. The clinicaltrials.gov ID is NCT4334148. It will be a double blind, placebo-controlled study of up to 15,000 health care workers at risk for COVID-19 exposure. There will be a baseline assessment using nasal swabs and a blood sample. The course of treatment will be 30 days with self-administered tablets of either HCQ or placebo with final nasal swabs and blood tests at the trials end. Eight weeks after the trial starts there will be a final contact between trial participants and those conducting the trial. Outcomes include adverse events and positive testing for COVID-19. Work exposures, such as in ICU, emergency departments, or respiratory services are required. Exclusion is for previous COVID-19 diagnosis. Contacts are 919-668-5590 and 919-668-4084.

Other efforts

A treatment that may be more effective than a drug (if it works) would be creating a vaccine using the blood plasma of those who have contracted COVID-19 and, having survived, have antibodies (immunity) so that when their blood plasma is injected into healthy persons, the antibodies act as a deterrent to infection or help to reduce the severity of symptoms.

Some experts suggest that COVID-19 might be around for some time, or perhaps even become seasonal, as influenza is. To have this method work well the antibodies would have to be "durable" and not disappear quickly from those who have survived infection. Should the antibodies not be durable, some experts also hope that those who have had infections may not get another infection if their immune system's T-cells (called "killer" T cells) can have the "memory," and perhaps the "muscle," to fight off new infections if the antibodies from prior infections don't endure.

Final notes

In an April 5 statement, the American Association of Pharmaceutical Scientists (AAPS) said that "pharmaceutical-research experts are raising concerns that attempts to offer desperate coronavirus patients some form of treatment may hobble crucial studies of which drugs actually work and which ones don't."

While these are not normal times for us or for the conduct of the clinical trials process, even as you read this, clinical trials for new drugs to fight cancer and other serious diseases may be grinding to a halt. Many, if not most, clinical trials are conducted on an "out-patient" basis where participants report physically to a trial site to be clinically evaluated for what their trial drug may or may not be doing for them, or to them. Comprehensive physical examinations and blood draws are important. Too important to miss. With social/physical distancing, in-person examination is difficult and telemedicine via Internet has limits in terms of examination. Thus, the hopes for surviving a serious disease by getting experimental drugs through a clinical trial may be now a fleeting experience, and for some time. And many drugs in the evaluation "pipeline" for future patients may not be able to proceed.

Finally, one knows these are not normal times because of the efforts to repurpose drugs to fit another disease, and do so with only a glimmer of hope. Also, one should know these are not normal times when political leaders, especially those political leaders who may have conflicts of interest with the test drugs, have enough power to preempt and bully scientists. The MDs and PhDs who conduct studies are required to have no conflicts of interest with the drugs they test. Further, they are responsible to IRBs, responsible for complying with approved practices and, foremost, responsible to – and for – their patients. Clinical trials principal investigators should not be held hostage by elected officials who have inflated egos but no clinical background or scientific training. ▪

Can Anyone Remember When Times Were Not "Uncertain?"

By Steve Smith
April 12, 2020

In recent weeks it seems like I've been exposed to around 1,200 advertising messages for everything from cars to carpet cleaners, all beginning with the phrase "In these uncertain times…" This cliché has become our new advertising contagion. Why don't they just get to the point? "We're open." "We're closed, but we're delivering." "We want you to buy a car and we're making deals." Ok, got it. But all this has made me think: Of what can we be "certain" these days?

Think about it – is it a certainty that our homes will increase in value? Previous generations were absolutely certain that being a homeowner was the realization of the American Dream. And equity in that home would enable a higher quality of life in many ways. Since the mortgage meltdown of 2005-2009, affectionately referred to as the "Great Recession," that traditional indicator of prosperity has been more "uncertain" than ever. Ask Millennials about this and they will express sincere doubts about home ownership as a sound investment.

Is it a certainty that any of our investments, even managed conservatively, will perform reasonably well? The financial markets, it seems, have been more turbulent than at any time since the Great Depression. And will corporate CEOs and their boards of directors be guided by sound policy with a long-term view, or will they continue their short-sighted pursuit of short-term gains? Or is it certain that the federal government will continue to bail out big corporations when they get into trouble? Perhaps one of the least likely certainties is that, following decades of offshoring, high quality manufacturing jobs will return to the United States.

In interpersonal relations, will there be a time when we can again be certain of shaking hands with someone – or even standing a bit closer to them – without thinking, "Is that person infected with the new plague?" Health experts say COVID-19 will be with us for some time, and that a resurgence is likely this fall.

In public policy, can we be certain that our government is not lying to us? That elected officials will do what is right for their constituency and not just what will get them re-elected? Wisconsin's April primary was a sad illustration of an electoral system pushed to the breaking point, and partisan politics resulting in citizens having to choose between their personal safety and their right to vote.

Can we be certain that policy makers will be guided by science and fact, and not by conspiracy theories or efforts to pander to the religious right, or the oil and gas industry, or both, just to get votes? Can we be certain the current occupant of the Oval Office always puts a higher priority on his TV ratings than he does on the substance and accuracy of information he delivers in the midst of a public health crisis?
The bigger question is – when will we, if ever, return to a time of "certainty?" Given that our society is as divided as it's ever been, is uncertainty our "new normal?"

Yes, that's another cliché. I feel helpless to say anything more. Stay healthy. ▪

PHOTO: American Red Cross volunteers from Detroit, Michigan during the 1918 Spanish Flu epidemic. Image courtesy Centers for Disease Control and Prevention, USA.

Unheeded Warnings: The WHO Bell Tolled, But Not Everyone Listened

By Randolph Fillmore
April 14, 2020

A study completed in September 2019 and compiled by the Johns Hopkins Bloomberg School of Public Health's Center for Health Security titled "Preparedness for a High-Impact Respiratory Pathogen," warns of the risks we would face in the event of a viral respiratory disease pandemic. Yes, like the one we now have. The 75 page, 2019 document predictively outlined exactly what has now transpired since the COVID-19 pandemic emerged early in 2020.

Commissioned by and prepared for the World Health Organization's (WHO) Global Preparedness Monitoring Board (GPMB) as a collaborative effort between WHO and the World Bank, the study outlines exactly – and in stunning detail – how we should respond if something like today's SARS-Cov-2/COVID-19 disease emerged. It also highlights what might happen if we don't get prepared as recommended. Most, if not all, of their dire predictions about our lack of preparedness have come true.

The GPMB, an independent monitoring and advocacy body, urges political action to prepare for and mitigate the effects of global health emergencies. Co-convened by the World Bank Group and the WHO, the GPMB works independently to provide assessments and recommendations for global preparedness.

The September 2019 document was meant to be a window into proper and expedient readiness but, reading it now, it becomes a mirror for inept behaviors, lack of preparation on the part of industry as well as medical and political institutions, and reflects greed, prejudice, xenophobia, and failed leadership on almost every front and in every category – and most seriously in the United States, the world's current leader in COVID-19 deaths.

The report accurately predicts a weak international response and subsequent damage, both to human health and national economies. The report defines, predicts and warns about what has transpired and continues to transpire in 2020, right down to shortages of medical equipment, the reckless promotion of unproven drugs, the economic disaster, and the irresponsible blaming of victims. It even looks in detail into the possibilities that something like a COVID-19 pandemic could be perpetrated as a weapon.

The findings of the report were summarized in the September 2019 WHO Annual Report.

On September 17, 2019, the GPMB issued a media release widely to inform the world's media about the report.

CNN ran the story on September 18. In the UK, *The Guardian* also ran the story on the same day.

Many news outlets that received the release did not run the story. I found the report by accident on Friday, April 10, 2020.

A quick Google search reveals some who passed the bad news along. The Kaiser Family Foundation covered the report in September 2019, as did the Homeland Preparedness News and the Australian Journal of Pharmacy.

The British medical journal *The Lancet* gave us a heads up on the report, but not until March 28, 2020.

"While WHO is under attack, their commissioning of this report in collaboration with The World Bank and through the GPMB, publishing it, and providing a more than adequate "heads up" to the international media, should help exonerate a distinguished and necessary body."

Making it clear that a serious respiratory outbreak is waiting to happen and is, perhaps, even overdue, the report specifically discusses the possibility of a novel coronavirus outbreak. The examples of the SARS 2003 outbreak and the 2009 H1N1 influenza are used throughout to point out the good and the bad of what was done and not done in 2003 and 2009, and make clear recommendations based on these recent serious outbreaks and the lessons learned in terms of what to look for, what to do, and what not to do.

Below are my edited and condensed summaries of report specifics, followed by more in-depth edited and condensed summaries of specifics should anyone care to continue reading.

What to do in preparation, even if no threat is imminent

National public health laboratories and large commercial laboratories should develop a concept-of-operations for how to distribute test kits rapidly to relevant clinical sites and laboratories in areas affected by the outbreak. Technological advances are needed to modernize our diagnostic capabilities to become faster and nimbler at the onset of outbreaks, particularly around novel pathogens.

Victims of a large-scale outbreak in settings with weak health systems would likely die at a higher rate than would be otherwise expected, due to lack of available modern medical care. Individuals who need to use the overburdened healthcare system for routine care during an outbreak would also likely suffer elevated morbidity and mortality, as available health resources are shifted to the emerging outbreak. (AUTHOR'S NOTE: Looking at this through the lens of today's reality makes the US health system look "weak.")

Isolation of the sick will be critically important to limiting further spread, but most hospitals around the world have very limited isolation capacity, particularly for airborne pathogens, and likely only a fraction of what would be needed in a large outbreak.

Stockpiles would ideally include not only basic supplies, such as IV tubing and fluid, but also disease-specific supplies, such as PPE (eg; gloves, surgical masks, N95 respirators, powered air-purifying respirators, or PAPRs), and medical countermeasures (eg; antivirals, antibiotics, vaccines).

Personal Protective Equipment (PPE), including masks and respirators, would also play a critical role in infection prevention and control, particularly if no vaccine or therapeutics are immediately available.

Mask suppliers would be besieged by countries and healthcare facilities around the world. If there were limited availability of masks and respirators in a given country equipment would need to be prioritized for health facilities to provide protection for healthcare workers and increase infection prevention and control measures. There is very little available information that studies the effectiveness of masks outside of health facilities. Additional research into the development of easy-to-use, effective, and reusable masks for wider use should be considered.

What to do to help limit and/or control the pandemic

(AUTHOR'S NOTE: Clearly the many distinguished and experienced experts who produced the report would want the World Health Organization (WHO) to take the lead on a respiratory, viral disease pandemic. It's what the organization was designed to do and what it has done, successfully for decades.)

Locally, the response should be centralized to a national government, not decentralized to states or counties. Quarantines work. Social distancing works. Wearing masks and gloves works. All three work best when they are implanted at the "get go," not weeks into a recognized pandemic. If people are quarantined by governments, those people have to be economically and nutritionally supported by those governments. There should be widespread testing. The health care industries should be at least a half step ahead in stockpiling PPE and at least have vaccine research in mind, given the SARs experience of 17 years ago.

Preparedness for high-impact respiratory pathogens will also require involvement from non-health actors, including other government, private, and nongovernment organizations. A response to a severe outbreak will increasingly need to incorporate actors from all sectors, including the private and business sectors. A review by the National Academy of Sciences specifically references the expertise of private and business sectors that can be utilized in response mechanisms, including operations, logistics, and supply chains.

Authorities may also need to provide frequent updates on any investigation into the outbreak's origins and advise against lashing out against others who "look like" they may have spread the disease.

If the pathogen is completely novel and there is no existing research base there is no alternative but to start with fundamental science and then advance through the development pipeline as quickly as possible.

Best to avoid these mistakes during a pandemic

Avert the uptake of fraudulent, life-threatening alternatives when access to the real beneficial countermeasure is impossible.

Conducting trials during an outbreak will be logistically and ethically challenging.

Manufacturers may face political pressure to produce vaccine for their home country before exporting to the rest of the world.

Quarantine measures will be least effective for pathogens that are highly transmissible, have short incubation periods, and spread through true airborne mechanisms, as opposed to droplets. As with travel restrictions, quarantine appears to delay the introduction of highly transmissible diseases but not prevent their spread entirely. Quarantine requires strict adherence to be effective.

In the "Twilight Zone" of disease where predictions come true

Below are bullet point highlights slightly edited and condensed from the report's lengthier statements, findings, and conclusions.

RISKS POSED BY HIGH-IMPACT RESPIRATORY PATHOGENS

- Novel pathogens continue to emerge, often first in animals with subsequent spillover into human populations living in close contact with animals. Global conditions enable pathogens to spread widely and quickly in people. International travel, mass displacement, migration, and urbanization enable pathogens to spread in new, susceptible populations. The rising incidence of chronic illnesses and drug-resistant infections place individuals at greater risk of infection and complications from respiratory viruses

- Novel high-impact respiratory pathogens have a combination of qualities that contribute to their potential to initiate a pandemic. If an infection is contagious in its incubation period prior to symptom onset spread will likely have taken place before awareness of the risk of the infection.

- Scientific developments have greatly advanced medical and public health tools to fight epidemic disease, but scientific developments have also created the ability for pathogens to be engineered or recreated in laboratories. Should countries, terrorist groups, cults, or scientifically advanced individuals create or obtain and then use biological weapons that have characteristics of a novel, high-impact respiratory pathogen, the consequences could be as severe as or greater than the consequences that would follow a naturally occurring pandemic with such pathogens.

Anticipating Challenges During the Deliberate Release of a High-Impact Respiratory Pathogen

- With advances in biology, a high-impact respiratory pathogen could be engineered to create transmissibility and lethality. The deliberate release of such a pathogen could substantially add to the already extraordinary consequences that would follow a naturally occurring pandemic event.

- A key difference between deliberate release scenarios and those in which a high-impact respiratory pathogen emerges and spreads via natural mechanisms would be the possibility for there to be multiple attacks, or "reload," in a deliberate event.

- Severe epidemics and pandemics have demonstrated how contagious disease emergencies can exacerbate societal divisions by fomenting social and political tensions and generating stigma against vulnerable groups who may be blamed. The potential for such negative societal consequences could be even worse in a deliberate event. Groups who are perceived as aligned with the perpetrator of an attack may experience backlash. Public fear and uncertainty could be high in the aftermath of a deliberate event, requiring highly effective risk communication and public outreach.

WHAT PREVIOUS REVIEWS TELL US ABOUT PREPAREDNESS FOR HIGH-IMPACT RESPIRATORY PATHOGENS

- The lack of global attention to – and consideration of – this threat illustrates the vital need to address preparedness for epidemics and pandemics that might be caused by high-impact respiratory pathogens.

- The implementation of border closures and travel bans may give governments more credibility among their own citizens for attempting to stop the outbreak, but historical evidence and modeling and public health experts would argue such measures would be unlikely to substantially add to disease control efforts.

- The leadership role and operational capabilities of WHO, which would be expected to lead in the event of a high-impact respiratory disease outbreak, have been widely examined and documented, specifically through the UN Panel on Protecting Humanity from Future Health Crises and the subsequent UN Global Health Crises Task Force.47,48 While most high-level reviews have reaffirmed the central role of WHO in outbreak response, they have also called for wide-ranging reforms, which culminated in the establishment of the WHO Health Emergencies Program.

- Multiple reports have recognized that a response to a severe outbreak will increasingly need to incorporate actors from all sectors, including the private and business sectors.

- A review by the National Academy of Sciences specifically references the expertise the private and business sectors contain that can be utilized in response mechanisms, including operations, logistics, and supply chains. Reports have noted that the support the private sector could provide would aid national governments in their preparedness planning and benefit responding agencies in streamlining activities such as procurement processes.

HOW CAN THE WORLD BETTER PREPARE FOR OUTBREAKS CAUSED BY HIGH-IMPACT RESPIRATORY PATHOGENS?

- The World Health Organization (WHO) leads the international response to major internationally important outbreaks, and it would be the lead agency for the health response to any high-impact respiratory pathogen event.

- International frameworks that have been conceived only within the past 20 years remain untested during a high-impact respiratory pathogen event that causes serious illness or death in tens or hundreds of millions of people or more.

- During a pandemic scenario, regional, national, and local needs could severely outpace existing international capacities and resources, and countries could not expect emergency medical response teams to assist them.

- In a large disease outbreak scenario, there may also be decreased international interest in supporting other countries' responses as nations deal with the health crisis in their own borders

- It remains to be seen the extent to which the global preparedness system will be prepared to respond to an epidemic or pandemic event caused by a high-impact respiratory pathogen. Individual country needs might quickly outstrip international resources and capacities, and national interests might overtake the imperative to adhere to international agreements on sample sharing, vaccine access, and emergency medical assistance. During a high-impact scenario, the limitations of current international frameworks would come into immediate focus.

- The Pandemic Influenza Preparedness (PIP) Framework provides a global approach to encourage influenza virus sample sharing and to commit manufacturers to equitably providing vaccines, treatments, and diagnostics during influenza pandemics and annually contributing funds to WHO for influenza pandemic preparedness.

- The capacity of organizations would likely be exhausted quickly, with little chance of replenishment due to high demand and scarcity of resources. Similarly, other countries would be focused on either combating the disease outbreak within their own borders or ramping up preparedness efforts to prevent the introduction of the disease into their territory. This may include decisions not to share vaccines with other countries until all domestic needs are met.

Multi-Sector Coordination and Involvement

- Preparedness for high-impact respiratory pathogens will also require involvement from non-health actors, including other government, private, and nongovernment organizations.

- A severe respiratory pandemic is likely to devastate economic growth, either directly via trade and travel restrictions or indirectly via high morbidity and mortality and the loss to jobs and industry, such as tourism. Therefore, both out of self-preservation and for reasons of corporate social responsibility, the private sector will need to play a greater role in planning for and responding to such events.

- The unique expertise and services of several industries deserve special attention. The first is the pharmaceutical industry, which plays a key role in the research, development, and manufacture of medical countermeasures. The second is the airlines, transportation, and logistics/ shipping industries, which can ensure the transfer of medical personnel and equipment for scaling up operations. The third is the medical supply industry, which would also be of high global importance in a pandemic and contribute to R&D and manufacturing of MCMs. And fourth is the global communications sector—both those who provide the hardware and software around communications, as well as those who are global leaders in delivering content and helping to serve public information needs. Despite its potential, private sector involvement to date has been haphazard and mostly limited to the response phase of a disease outbreak. A key challenge is the lack of advance communication and coordination between public and private actors.

Surveillance, Monitoring, and Assessment Systems

- In addition to assessing the availability of laboratories that can perform diagnostic testing, countries must also consider the capacity of laboratories to handle testing in the event that there is a large surge in demand, efforts should be made to further strengthen these mechanisms and improve laboratory testing.

- In an event involving a novel pathogen, national public health laboratories and large commercial laboratories should develop a concept-of-operations for how to distribute test kits rapidly to relevant clinical sites and laboratories in areas affected by the outbreak.

- Technological advances are needed to modernize our diagnostic capabilities to become faster and nimbler at the onset of outbreaks, particularly around novel pathogens.

- Diagnostics become an important tool in event characterization (determining who is affected, who is at risk of severe outcomes) and in clinical management of patients to optimize treatment and to reduce transmission through proper isolation.

Health Systems and Infrastructure, Health Services, and Clinical Management

- Victims of a large-scale outbreak in settings with weak health systems would likely die at a higher rate than would be otherwise expected, due to lack of available modern medical care. Individuals who need to use the overburdened healthcare system for routine care during an outbreak would also likely suffer elevated morbidity and mortality, as available health resources are shifted to the emerging outbreak.

- Early in a pandemic, isolation of the sick will be critically important to limiting further spread, but most hospitals around the world have very limited isolation capacity, particularly for airborne pathogens, and likely only a fraction of what would be needed in a large outbreak. To adequately prepare for and respond to outbreaks of respiratory pathogens, health facilities would need to increase their capacity for large-scale isolation of patients with highly transmissible respiratory diseases.

- There is a severe maldistribution of medical supplies between countries and health systems around the world, and a dedicated effort is needed to determine how low- and middle-income countries would maintain access to critical supplies (eg; masks, respirators, gloves, gowns, IV fluid bags, medical gases) during a large-scale respiratory disease outbreak.

Community Engagement

- Community engagement includes creating bridges, open dialogue, and mutual understanding among clinical trial participants, communities, and investigators, thus furthering research will help in achieving collective behavior change, such as alterations in burial practices, social gatherings

Risk Communication

- Apart from having to employ effective public education to dampen people's impulses to shun affected individuals or groups during the outbreak for fear of disease, for example, authorities may also need to provide frequent updates on any investigation into the outbreak's origins and advise against lashing out against others who "look like" they may have spread the disease (in the event of a naturally occurring pandemic) or those who might be presumed perpetrators (in the case of a biological attack.

- Risk communication dilemmas may include how to inform peoples' choices about uptake when they fear a seemingly "rushed" drug or vaccine, how to elicit public confidence in decisions about the allocation of a very scarce life-saving countermeasure, and how to avert the uptake of fraudulent, life-threatening alternatives when access to the real beneficial countermeasure is impossible

Communication With the Public

- Risk communication also includes communication with and through intermediaries such as trusted on-the-ground partners and the news media in order to leverage their capacity as amplifiers of appropriate risk and protective action messages. Although there are many fundamental differences between these different groups, they both act as message mediators and require dedicated time and effort to build relationships and partnerships over time. Trusted partners may also act as advocates during times when public trust in public health is low and misinformation is rampant.

Medical Countermeasures and Pharmaceutical Interventions

- Personal Protective Equipment (PPE), including masks and respirators, would also play a critical role in infection prevention and control, particularly if no vaccine or therapeutics are immediately available.

- National and local governments, academic institutions, the pharmaceutical industry, and the private sector would need to move products through early and advanced development and the regulatory process, the manufacturing and finishing processes, and the distribution and dispensing systems needed to administer countermeasures to people who need them.

- Perhaps a coronavirus vaccine for an existing coronavirus could be used with some value for a novel coronavirus that causes high-impact respiratory outbreak), there is likely to be no surge manufacturing plan or capacity. If the pathogen is completely novel and there is no existing research base—what WHO refers to as a Disease X scenario—there is no alternative but to start with fundamental science and then advance MCMs through the development pipeline as quickly as possible.

- Attempts at developing vaccines against respiratory pathogens such as SARS coronavirus have been slow. Technical barriers at the discovery and R&D phases of development or market failures can be rate limiting. Once a candidate drug or vaccine has been developed, it must then go through clinical trials to test for safety and efficacy. However, trials during an outbreak will be logistically and ethically challenging. Moreover, many countries maintain their own paradigm for pharmaceutical regulation and have not put in place policies for emergency use of medical countermeasures that may not have full regulatory approval. These

complexities could slow international MCM deployment, which could impede efforts to control a severe disease outbreak.

- What is needed, but is not currently possible, is the capability to get MCMs from discovery to mass administration within a few months. Because there is very little surge capacity in the system, companies would be faced with taking commercial vaccine production offline in order to accommodate vaccine for the new pathogen. Also, manufacturers may face political pressure to produce vaccine for their home country before exporting to the rest of the world.

- Widespread use of masks and respirators by the public would be complicated by the challenges of proper fit, the costs, and the inability of the supply chain to provide masks at that scale. The same mask suppliers would be besieged by countries and healthcare facilities around the world. If there were limited availability of masks and respirators in a given country (which would be highly probable), they would need to be prioritized for health facilities to provide protection for healthcare workers and increase infection prevention and control measures. Beyond this, in the public setting, there is very little available information that studies the effectiveness of masks outside of health facilities. Additional research into the development of easy-to-use, effective, and reusable masks for wider use should be considered.

The Economics of Medical Countermeasure Development

- In the United States, which has the largest pharmaceutical market in the world, only 13% of new drugs approved between 2005 and 2016 were novel drug products.

- It is necessary to consider different avenues for promoting research and development of medical countermeasures for respiratory transmissible diseases with pandemic potential. Regulatory, policy, tax, and direct financial incentives have all been used at various times and could be pursued further to encourage R&D investment by industry.

Nonpharmaceutical Interventions (NPIs)

- **Travel restrictions** refer to enforceable limitations on travel but should not be confused with travel alerts or notices, which provide information for travelers on ongoing health events. Studies have found that travel restrictions would be less effective once a disease has spread to multiple geographic areas or been introduced to large cities.

- **Movement restrictions** are measures implemented to prevent or limit contact between infectious individuals and susceptible populations, ranging from limits on how or where an individual can travel to full quarantine.

- **Quarantine** is a separation of potentially infectious individuals from susceptible populations. It is often confused with isolation, which refers to separating individuals known to be transmissible (typically implemented in a health facility). Though isolation is routinely used in healthcare and public health practice, the use of quarantine is rare and has been controversial. For a high-impact respiratory pathogen, quarantine may be the least likely NPI to be effective in controlling the spread due to high transmissibility. Quarantine measures will be least effective for pathogens that are highly transmissible, have short incubation periods, and spread through true airborne mechanisms, as opposed to droplets. As with travel restrictions, quarantine appears to delay the introduction of highly transmissible diseases but not prevent their spread entirely. Quarantine requires strict adherence to be effective, **so it works best when government has a trusting relationship** with the public. Quarantine and other movement restrictions also involve legal and ethical considerations and should be supported by available evidence to prevent undue burden on affected

individuals. The government must have both the legal authority to quarantine individuals and the operational ability to enforce quarantine orders. Quarantine is being considered include the responsibility for ensuring the safety of affected individuals that are quarantined and providing medical, communication, and legal services as well as food, shelter, and other necessary supplies.

- Social distancing covers an array of measures aimed at reducing contact between members of the community that could potentially result in disease transmission, including closing schools, canceling mass gatherings, facilitating remote- or tele-working, and suspending mass transit operations. Monitoring and enforcing some of these NPI measures would be quite difficult if not impossible, due to the inability to fully monitor large communities and address noncompliance issues. The disruption of normal activities such as schools closing may result in children congregating elsewhere, thus making social distancing efforts irrelevant.

- It is important to communicate to political leaders the absence of evidence surrounding many NPI interventions and the adverse consequences that may follow them.

Deliberate Use and Biosecurity

- When considering the possibility of a deliberate release of a novel high-impact respiratory pathogen, the exact properties of the pathogen and its transmission dynamics would be uncertain, ranging from synthesis of a known virus to the creation of an engineered strain with highly unexpected properties. Deliberate release scenarios are more complex than natural epidemics because they would be initiated by an attacker who chose where and how to attack for a purpose.

- Some RNA viruses may particularly lend themselves to natural pandemic spread, but they are currently hard to engineer, particularly with trans genes. It is reasonable to predict that the barriers to such engineering will decrease in the future. Rapid advances in synthetic biology capabilities, such as nucleic acid synthesis, increase the possibility that pathogens could be engineered to meet specific objectives of a sophisticated attacker.

- Advances in synthetic biology capabilities have driven innovation in the life sciences and created novel capabilities and novel risks. One such capability is nucleic acid synthesis, which has enabled the creation of new therapeutics

CONCLUSIONS: STRENGTHENING PREPAREDNESS FOR A HIGH IMPACT RESPIRATORY PATHOGEN PANDEMIC

- Countries should continue to build and improve core public health capacities across the globe and ensure that WHO has the resources it needs to continue to play a coordinating role. WHO should continue to work to ensure that core capacity strengthening is viewed as a matter of priority by leaders.

- Even the most robust public health surveillance systems are unlikely on their own to provide enough information to inform the wide range of decisions that would need to occur during an epidemic or pandemic response.

- Countries should assess the readiness of health facilities to effectively treat patients with a transmissible disease with high case fatalities. WHO should work with member countries to develop a corresponding assessment tool for health systems and facilities, so that countries have a means of assessing the readiness.

- Countries should plan for the possibility of there being interruptions in the availability of essential basic

supplies and equipment. Health facilities would need plans for continuing operations in the event that supplies are no longer available from their primary sources.

- Stockpiles would ideally include not only basic supplies, such as IV tubing and fluid, but also disease-specific supplies, such as PPE (eg; gloves, surgical masks, N95 respirators, powered air-purifying respirators, or PAPRs), and medical countermeasures (eg; antivirals, antibiotics, vaccines).

- There are a range of promising approaches to accelerate rapid vaccine development that should be concomitantly pursued and funded, given the uncertainty in knowing which might bring the most important leaps forward. Traditional vaccine development through big pharma and biotech companies will continue for now to be the backbone of the field. Nucleic acid (RNA and DNA)–based vaccines are widely seen as highly promising and potentially rapid vaccine development pathways, although they have not yet broken through with licensed products.

- Many countries maintain their own paradigm for pharmaceutical regulation, and significant regulatory challenges are associated with deconflicting the regulatory processes across countries, but many countries lack tools to limit manufacturer liability during a crisis. These complexities will slow international MCM deployment and impede efforts to control an outbreak as it begins to spread around the world.

- Many NPIs, particularly those falling under social distancing, require support and acceptance by the public. As these measures inherently limit civil liberties by restricting individuals' movements, assembly, and social interaction, they can be a source of substantial opposition from affected individuals and populations. Providing strong evidence-backed reasoning for the necessity of NPIs, including the predicted impact they will have in containing the outbreak will be crucial.

- Any attacker that successfully deploys a bioweapon (as opposed to conventional weapons) should be presumed to have substantial biological scientific abilities, particularly if it is discovered that the pathogen has been engineered. If a bioweapon is used that causes a high-impact respiratory epidemic or pandemic, that would suggest a great degree of capability and sophistication in the attacker. Such an attacker might try to improve the chance of success by deploying the bioweapon simultaneously in multiple locations. It may be that such an attack is done without claiming responsibility, or without public notification that a release has occurred. Widespread dissemination of a bioweapon could overwhelm traditional outbreak surveillance and control efforts.

- Synthesis of coronaviruses and novel influenza strains should also require special review of the proposed work and the proposed buyer before approval. The US government provides guidance on synthesis screening. It is not a perfect approach for preventing the illicit synthesis of high-impact respiratory pathogens, because it focuses on the US select agent list, which does not necessarily include the viral components of greatest concern for this problem.

- Finally, a deliberate release event that results in a pandemic spread of a respiratory pathogen would require a high level of sophisticated coordination to bring the outbreak under control. One or two governments could not accomplish this effort without working in close concert with other governments and international organizations. ▪

Responsibility, Ethics and Morality During the COVID-19 Pandemic

By Randolph Fillmore
May 15, 2020

In 2007, the World Health Organization (WHO) issued a report titled Ethical considerations in developing a public health response to pandemic influenza. While the report focused on an influenza pandemic rather than a coronavirus pandemic, a viral pandemic is a viral pandemic.

The purpose of the WHO 2007 report was to "assist social and political leaders at all levels who influence policy decisions about the incorporation of *ethical considerations* into national influenza pandemic preparedness plans." The document focuses on priority-setting and equitable access to resources, restriction of individuals' movements as a result of non-pharmaceutical interventions, including isolation of cases, quarantine of contacts, limiting social gatherings, and highlighting the obligations of health care workers, their employers and governments.

In 2007, WHO said "…implementation of public health measures aimed at limiting social interaction (such as restrictions on gatherings and population movements) are likely to have a major impact on trade and tourism. In view of these possible consequences, countries and the international community must prepare to cope with a pandemic and mitigate its impact."

Many critical ethical questions arise in viral pandemic planning, preparedness and response. According to WHO, these questions include: Who will get priority access to medications, vaccines, and intensive care unit beds, given the potential shortage of these essential resources? In the face of a pandemic, what obligations do health-care workers have to work, notwithstanding risks to their own health and the health of their families? How can surveillance, isolation, quarantine and social-distancing measures be undertaken in a way that respects ethical norms? What obligations do countries have to one another with respect to pandemic influenza planning and response efforts?

WHO went on to say that authorities imposing social distancing/quarantine orders have ethical and moral obligations to provide "employment protection" for workers who comply with social distancing measures and that social distancing plans require authorities to take measures to mitigate adverse cultural, economic, social and emotional health effects on individual and communities (to the extent possible) resulting from social distancing or quarantine.

Is it unethical for employers to demand health care workers work without adequate protection?
WHO said health care workers do have a "moral obligation to work" during a pandemic, but that the obligation is not "unlimited." WHO said health care facilities have an ethical obligation to provide personal protective equipment (PPE) "in line with technical advice" and, additionally, that health care workers had an obligation to use the PPE.

Recall there have been several cases of nurses who refused to work without proper PPE, resulting in their dismissal.

"I don't believe it is unethical for health care workers to say they are not going to work if they don't have personal protective equipment," says Alison Bateman-House, PhD, an assistant professor in New York University's Department of Population. "We can't demand people to self-sacrifice. It was unethical to penalize those workers."

Health care workers are not the only ones under the COVID-19 "gun." Meat packing plant workers have been ordered to go back to work, although the workers say they do not have proper PPE. One hopes they can appeal to a Higher Authority – OSHA – the Occupational Safety and Health Administration. Born in 1970 with the Occupational Safety and Health Act, OSHA says that "workers have the right to a safe workplace."

One section on the OSHA website highlights OSHA standards and directives (instructions for compliance officers) and other related information that may apply to worker exposure to the novel coronavirus, SARS-CoV-2 that causes Coronavirus Disease 2019 (COVID-19). Among the most relevant aspects are OSHA's Personal Protective Equipment (PPE) standards (in general industry, 29 CFR 1910 Subpart I), which require using gloves, eye and face protection, and respiratory protection when job hazards warrant it. There is also guidance for when respirators (masks) are necessary to protect workers. Employers must implement a comprehensive respiratory protection program in accordance with the Respiratory Protection standard (29 CFR 1910.134). This may not be happening, as it appears that when employers call employees back to work it may not be in keeping with OSHA regulations.

Who gets a ventilator, who does not?

Early in the pandemic, the nation-wide shortage of ventilators – the "breathing machines" that force oxygen into the lungs and help keep people with failing lungs alive – became apparent. Some estimates were that the U.S. would need millions when only about 100,000 ventilators existed nationally.

Some of the earliest COVID-19 "cures" came when the sickest of people were placed on ventilators and "breathed" for a rather long time. However, many of those placed on ventilators died anyway. Given the ventilator shortage, does that reality mean that it could have been determined that this person was so sick and so close to death that putting them on a ventilator was futile? Perhaps someone else could have been put on that ventilator and lived to tell about it.

Ethical controversy over ventilators gained more momentum, albeit temporarily, when a paper published in the Journal of the American Medical Association (JAMA) on April 22 said that 88% of those placed on ventilators in New York City died, regardless.

Two days after publication, JAMA put out a correction based on an overwhelming number of medical experts who over two days commented that there was something wrong with the data. The correction said that 24.5 % (282) of the 1100-plus patients on ventilators died. Not 88%. Even with this correction, the question remains open as to who should be put on a ventilator and who might not be a candidate given the simple fact that everyone who might be a candidate could not get one. It's a tough, "lifeboat" decision about who lives and who dies. "First-come-first-served is an allocation of its own," says Bateman-House. "But in this case, it might not be a random cross section of the population. Questions about 'who can afford the care, who can get transportation to the hospital, and who has a cell phone to call 911?' are issues."

What is a doctor to do?

"It might be best to do what doctors tend to do – and that is make individual determinations about patient

changes and maximize the care to those with the best changes," suggests Bateman-House. "Does the data show signs that this patient is not going to survive? Data enables us to come up with protocols."

Looking at the data for making these kinds of ethical decisions is what researchers at the Johns Hopkins University and the University of Pittsburgh did in collaboration in 2013. Their study into ventilator use/triage became solid guidelines that could be put in place when necessary, and likely deemed ethical. Or not. Under the subtitle: "Categorically Excluding Large Groups of Patients from Receiving Mechanical Ventilation Is Ethically Problematic," researchers published a paper in JAMA on 20 April 2020 looking at a framework for rationing ventilators and critical care beds during the COVID-19 pandemic.

The original 2013 report suggested a ventilator allocation based on saving as many lives as possible in two ways: the likelihood of short-term survival enabling the patient to leave the hospital; and the likelihood for long-term survival of at least 12 months.

The 2013 report is now a framework living deep within the pages of the University of Pittsburgh's website.

Here is what the framework says: When ventilators are a scarce commodity, prospective ventilator patients are scored for suitability on an 8-point system. Short-term survival is based on an adult patient's organ failure assessment score using laboratory values and organ function indicators. For long-term survival, patients needed to score from 0 to 3 and would be "high priority." Those patients likely to die within one year would be scored a 4-5 and would be intermediate priority. Scores of 6-8 would be the lowest priority. The scores would be computed by a qualified "triage team" and reassessment could be done in any of the three categories. The teams are also open to "appeals" from the patient's family. With borderline scores, age can also be a determining factor.

The framework explains reassessment:

"The ethical justification for such reassessment is that, in a public health emergency when there are not enough critical care resources for all, the goal of maximizing the benefit for communities of patients would be jeopardized if patients who were determined to be unlikely to survive were allowed indefinite use of scarce critical care services. In addition, periodic reassessments lessen the chance that arbitrary considerations, such as when an individual develops critical illness, unduly affect patients' access to treatment."

Going ethically and morally forward into 2021's unknowns

The Center for Infectious Disease Research and Policy at the University of Minnesota released a report 30 April 2020 saying "…the length of the pandemic will likely be 18 to 24 months, as herd immunity gradually develops in the human population…we must be prepared for at least another 18 to 24 months of significant COVID-19 activity, with hot spots popping up periodically in diverse geographic areas. As the pandemic wanes, it is likely that SARS-CoV-2 will continue to circulate in the human population and will synchronize to a seasonal pattern with diminished severity over time." https://www.cidrap.umn.edu/covid-19/covid-19-cidrap-viewpoint

One of the center's recommendations is that "risk communication messaging from government officials should incorporate the concept that this pandemic will not be over soon and that people need to be prepared for possible periodic resurgences of disease over the next two years."

If this drags on for years, or if a new pandemic takes over where this one left off, or we have more than one pandemic at a time, what should we stop doing, and what should we start doing to responsibly improve the ethical and moral public health response?

Things to Start doing if (or before) CDC declares an epidemic or if WHO declares a pandemic

We should de-politicize pandemic response to the extent possible taking pandemic response - including quarantine and drug research - out of political hands and put it entirely into the hands of the directors of the U. S. Centers for Disease Control and Prevention (CDC) , the U.S. Food and Drug Administration (FDA), the Biomedical Advanced Research and Development Authority (BARDA), and the US Public Health Service (USPHS).

- If quarantine is warranted, take economic care of those stuck at home, especially those left unemployed
- Allow the WHO/World Bank Global Preparedness Monitoring Board (GPMB) https://apps.who.int/gpmb/about.html to play a role in determining outbreak seriousness and advise in steps to reduce outbreak effects
- Nationalize health care materials production and distribution in serious health emergencies
- Develop a national health crisis unemployment fund; repurpose and pay workers to do pandemic-related tasks (off-label work?) for which they will be trained during non-pandemic times
- Boost and accelerate federal funding of continuous vaccine research, both influenza, corona, Dengue fever and others, and have continuous, forward-looking development and full phase 1-3 clinical trials on new drugs rather than on re-purposed drugs

Conclusion

The Biomedical Advanced Research and Development Authority (BARDA), part of the HHS Office of the Assistant Secretary for Preparedness and Response, was established to aid in securing the nation in times of chemical, biological, radiological, or nuclear (CBRN) threat, as well as reacting to pandemic influenza (PI) and emerging infectious diseases (EID). https://www.phe.gov/about/barda/Pages/default.aspx

BARDA's important mission is to support the development and application of medical countermeasures, such as vaccines, drugs, and diagnostics. BARDA's mission extends from research through advanced development towards consideration for approval by the FDA and, ultimately, to inclusion of medically appropriate products into the Strategic National Stockpile.

That BARDA has been stifled from carrying out its mission should be considered an immoral and unethical political maneuver. It should be alarming to all Americans as such a move stands as an example of the extreme politicizing of a critical federal government functional unit aimed at preserving the health and welfare of all citizens in times of serious natural or human-made threats. ▪

Emerging From Your COVID-19 "Cocoon"

By Steve Smith
June 12, 2020

While working at home, meeting via video conference, wearing face masks and just plain staying home, many of us are thinking: How will my business emerge from this crazy thing? Smaller? Smarter? Unrecognizable? It's a safe bet that in many ways you and your organization will never be the same.

On a video conference the other day, one of the participants reminded our group of what we all should be doing – figuring out how we and our businesses will be different when reopened and released from our "Coronavirus Cocoons."

Admittedly the overused phrase, "We're all in this together" does apply here. Every business in North America, and around the world, nonprofit or for-profit, should be considering how it will emerge from the strange-but-true reality of the coronavirus.

As business owners prepare to reopen, they're asking, "Am I ready? Will my consumer communities be receptive, or apprehensive?" How will their needs change? How will changes in our social norms affect my relationship with them?

Will you be like a tempest-tossed Dorothy Gale opening the door from her black-and-white, post-twister wreckage onto a candy-colored Munchkin landscape? Or will you be looking at more of a post-apocalyptic, I Am Legend / Omega Man scene?

Given the fact that the pandemic has been so completely politicized, how do you appropriately reach people who think the pandemic is overblown and those who think we aren't responding as responsibly as we should? Ryan Phelan's Marketing Land article sheds some light on this and offers advice.

Now is not the time to go dark

Think now about how to implement content marketing tactics that will pay off later. Keep the storytelling "drumbeat" going. Carefully consider what meaningful and memorable stories you want to share. Stories about first responders and COVID-19-related heroism are great for the moment, but the moment will pass. It's important to share stories that bring it back to your mission.

Going a step further, now is the time to do the planning you didn't have time to do during "normal" times. For example, how about finally documenting your Content Marketing Strategy? Or what about some soul-searching to redefine your positioning strategy? Is your website in good shape, or in need of a long-overdue makeover. Maybe now is the time to study the feasibility of new distribution channels or new markets.

Time to Make a Fresh Start?

For many, this will be an opportunity for a fresh start. In many ways it's an opportunity to re-think, recalibrate and perhaps start over. During the "Great Recession" of 2008-2009, many business owners did just that. It was a time to re-think everything, throw out what wasn't working and usher in a new way of doing things.

Looks like that time has come around again. ▪

As Coronavirus Rages, Florida Plays Politics

By Steve Smith
July 16, 2020

Florida is now the epicenter of the coronavirus pandemic, with 15,300 new cases reported this week the highest single-day total yet in any U.S. state and a quickly diminishing supply of ICU beds, but partisanship has prevented the implementation of a mask mandate, which health experts say could save thousands of lives. Gov. Ron DeSantis extended the state of emergency for the pandemic on Tuesday for another 60 days.

During that same 60-day period, several public events are planned for Florida that have super-spreader potential. The NBA is scheduled to restart its season in Orlando, the Republican National Convention is slated to take place in Jacksonville, schools are supposed to open, a primary election will be held and colleges will be back, perhaps with football on their campuses. All while the pandemic rages and our so-called leaders play politics.

As reported by the Orlando Sentinel and others, the state has now become a major hotspot, with 2,700 cases per 1 million in population over the first seven days in July, according to a New York Times analysis, second only to Arizona with 3,300 in that time.

On July 12, Florida reported 15,300 new COVID-19 cases, the highest-single day total in the U.S. since the pandemic began. In all, the state now has reported 302,000 cases and 4,520 deaths.

On July 14, the state posted another new record high death toll.

Facemasks remain a "personal choice"

Despite reporting more new cases than all of Europe combined and 52 hospitals with maxed out intensive care unit capacities, Florida Governor Ron DeSantis has continued to insist he will not institute a state-wide mask mandate, saying he trusts Floridians to make "the right decisions," even with the evidence that "widespread noncompliance" with coronavirus guidelines led the state to shut down reopened bars and restaurants last month.

Our Governor's "make the right decisions" statement is the latest sidestepping maneuver by a politician seeking to maintain favor with his conservative base and perhaps to perform to an audience of one, namely Donald Trump, who campaigned enthusiastically for DeSantis' election.

Were all those people crowding into bars and nightclubs and attending massive private house parties in recent weeks making "the right decisions?" If they had been, they would have stayed home and not passed along the virus to friends, co-workers family members and each other.

As a result of inaction at the state level, a patchwork of local ordinances is taking shape. For example, the city of Bradenton is joining other local governments, including the city of Sarasota, Holmes Beach, Anna Maria Island and Longboat Key, in issuing a mask ordinance. Starting Friday, July 17, businesses will be required to display signage encouraging the public to wear masks.

However, although business owners that don't post signage are subject to a warning and potentially a $75 fine, the ordinance does not mandate that they enforce mask-wearing: "Nothing contained herein shall be construed to mandate the wearing of face coverings nor require the owner or operator of any business establishment to mandate or otherwise enforce the wearing of face coverings," the order says.

On July 8, Florida Sen. Linda Stewart became the latest to publicly criticize the lack of a statewide order as "irresponsible," joining calls from thousands of Florida physicians, the state's agriculture commissioner and progressive policy groups for an immediate mandate.

Facemasks remain highly unpopular in parts of Florida where local mandates have sparked lawsuits and anti-mask protests on the basis that these requirements infringe upon personal freedoms.

Florida Republican state lawmaker Rep. Anthony Sabatini, who has filed numerous lawsuits to prevent mask mandates in his state, told CNN's Brianna Keilar that his state is "doing just fine" despite data showing Florida is the new epicenter of the coronavirus.

He also told Keilar and her viewers that he doesn't bother to wear a mask when he's in public because maintaining social distance is enough.

A dereliction of duty

This failure to enforce face coverings is just the fractured and dysfunctional approach you get when you ignore the science-based advice of public health officials and allow political partisans to call the shots.

As if this wasn't absurd enough, DeSantis is pushing forward the Trump administration's directive to fully open schools for the fall semester. The pretzel logic of politics demands, after all, that if we can open up the Walmart and Home Depot, then we certainly can open up the schools. Sure, because your kids and mine normally spend around seven hours each day in a big box retail store.

And come election day, will Floridians be allowed to cast their votes by mail, or will we see another, even larger, version of the scene played out in Wisconsin's primary election – the long lines of people standing out in the weather for hours and risking their health just to exercise their right to vote.

I have often said Florida is around 47th in everything except politics and bullshit. The state's failed response to the coronavirus pandemic has finally made the Sunshine State Number One in something.
Congratulations, Florida. You're finally a leader. ▪

Breast Cancer Treatment in the Age of COVID-19: The Doctor Will Zoom With You Now

By Randolph Fillmore
October 13, 2020

With this year's observance of "Breast Cancer Awareness Month," breast cancer awareness and concern about optimal treatment has come with an unwanted "October surprise." Early in the pandemic it became clear that cancer care needed to be modified to reduce the risk of COVID-19 infection for both patients and their health care teams. But COVID-19 is still around.

How is the nasty virus affecting, or not affecting, breast cancer diagnosis and treatment?

Surprisingly (or unsurprisingly) experts do not agree. With telemedicine and video conferencing playing a strong role, some say breast cancer treatment is, for the most part, unaffected by COVID-19. Others say that treatment has been "quite affected" by COVID-19 with treatment and patient follow-up dependent on "virtual medicine" via "telemedicine" but may not substitute for the doctor/patient up close and personal experience.

Questions have also been raised regarding whether breast cancer patients have been happy with the Zoom results or really miss that "personal touch." For breast cancer patients, this is an ongoing important issue going forward as the pandemic, at least in the US, appears not to be slowing down.

Zoom or doom and gloom?

In an American Society of Clinical Oncology (ASCO) online commentary, Carolyn B. Hendricks, MD, self-described as a "breast-dedicated medical oncologist" in community practice in Bethesda, Maryland, wrote a commentary titled "The Doctor Will Zoom With You Now: Telemedicine and Breast Cancer Care."

"The most significant change has occurred with the rapid transition to telemedicine," wrote Dr. Hendricks. "Telemedicine is loosely defined as caring for patients remotely when the doctor and patient are not physically present with each other. Telemedicine has its history in rural medicine. Telehealth visits were originally envisioned for patients living in rural areas. But initially, the patients were in health care facilities for these visits, not in their own homes. Prior to the COVID-19 pandemic, many cancer centers and oncology researchers were studying ways to deliver cancer care via telemedicine in pilot projects. The COVID-19 pandemic sped up the process dramatically."

Dr. Hendricks said her group practice adopted telemedicine using a licensed Zoom platform in March of 2020. "My proportion of televisits grew rapidly to approximately 30 percent," she wrote. "The proportion has waned somewhat, but it remains about 20%. This option is made available to all my patients, including new patients. Fortunately, my practice has had a very low incidence of COVID-19–positive tests among my patients, their families, and my staff. The option of televisits has helped to reduce this risk, particularly in my highest-risk

patients whose immune systems are affected by their cancer treatments, as well as for my patients who have vulnerable family members in their households. It has also helped to overcome the severe visitor restrictions that COVID-19 has imposed on our in-person visits."

According to Dr. Hendricks, Zoom visits typically require more advance preparation by doctors, the doctor's staff, and the patient, but Zooming seems to work pretty well.

"My patients can tell that I am fully engaged with them during the time that we share. Because the visits are timed and staggered, there are very few interruptions on either end," she adds. "I feel very comfortable meeting new patients and outlining a treatment plan via televisit."

Do patients miss the personal touch?

Also offered during an ASCO virtual meeting was an analysis of telemedicine visits by health care providers at the Tel Aviv Medical Center and Sackler School of Medicine, in Tel Aviv, Israel.

"Almost all ambulatory activity in the oncology division in Tel Aviv Medical Center was converted to telemedicine services," said the authors, who conducted a telephone interview questionnaire assessing patient satisfaction. Inclusion criteria included solid tumor patients over 18 years of age who utilized the telemedicine platform at Tel Aviv Sourasky Medical Center between March 2020 and May 2020. Survey aimed at evaluating patients' perspectives and preferences regarding telemedicine and assess whether virtual communication affected the patient-doctor relationship.

The authors reported that 100 patients participated in the survey. The majority of patients independently downloaded the telemedicine application and did not encounter technical constraints and almost half had family members and friends attending telemedicine visits. Of those surveyed, 18 percent were breast cancer patients. Visit intent included post-treatment follow up (40%), active treatment follow (53%), and first visit intake (7%). The majority of patients felt their emotional needs were met (88%) and said that their treatment was not harmed due to absence of a physical visit (84%). Ninety-nine percent felt their privacy was maintained and 95 % of patients affirmed that the virtual visit relieved their worries regarding treatment interruption; 75% of patients affirmed their interest to continue telemedicine regardless of COVID-19 pandemic.

Triage

In a paper published in the April 20 issue of the journal *Breast Cancer Research and Treatment,* titled "Recommendations for prioritization, treatment, and triage of breast cancer patients during the COVID-19 pandemic" the authors said that the COVID-19 pandemic presented clinicians with "a unique set of challenges in managing breast cancer patients."

They noted that as hospital resources and staff became more limited during the COVID-19 pandemic, it became critically important to define which patients required more urgent care and which patients could wait for treatment until the pandemic ended.

The authors used the expert opinions of representatives from multiple cancer care organizations to triage breast cancer patients into priority levels (A, B, C) for urgency of care across all specialties and provided treatment recommendations for each of these patient scenarios. Priority A patients had conditions that are immediately life-threatening or symptomatic requiring urgent treatment. Priority B patients had conditions that did not require immediate treatment but should start treatment "before the pandemic is over." Priority C patients had conditions that could be safely deferred until the pandemic is over.

Implementation of these recommendations for patient triage was based on the highest-level evidence available "adapted to current availability of hospital resources and severity of the COVID-19 pandemic in each region of the country," said the authors.

Additionally, the risk of disease progression and worse outcomes for patients had to be weighed against the risk of patient and staff exposure to COVID-19.

A study looking at COVID-19's impact on breast cancer care delivery early in the pandemic at the Columbia University Irving Medical Center in New York City was also found on the ASCO virtual meeting site.

"We aimed to characterize breast cancer patients without COVID-19 whose care was impacted by the COVID-19 pandemic at an academic center in New York City," said the authors who performed a retrospective cohort study of breast cancer patients treated at a medical oncology practice between February 1, 2020 and April 4, 2020. Patients were included if they were scheduled to receive intravenous or injectable therapy or were scheduled as a new patient. Patients were excluded if they tested positive for COVID-19 or transferred care during the study period. Delays were defined as postponements of scheduled care and changes were defined as care alterations without postponements. Impact on care was defined as any change or delay in any oncologic care for which a patient was scheduled.

The study found that nearly half of the breast cancer patients experienced a change or delay in workup or treatment and, once more, "significant racial and socioeconomic disparities" impacted care.

Conclusion: Hopes for next year

October 2020 has found that, by-and-large, the medical community adapted to giving the best care possible to breast cancer patients virtually, but that conclusion may be premature as the several studies available may not be representative of a bigger picture over the length of the COVID-19 emergency. Only a retrospective look once the pandemic is over will tell the true story. Breast cancer patients and their families can only hope that a return to normal is not more than another October "Breast Cancer Awareness Month" away. ▪

Resources:

https://www.esmo.org/guidelines/cancer-patient-management-during-the-covid-19-pandemic/breast-cancer-in-the-covid-19-era

https://moffitt.org/patient-family/moffitt-virtual-visits/?utm_source=moffitt&utm_medium=tile&utm_campaign=tilereview21

https://www.breastsurgeons.org/management/practice/covid19

What is Factor D?

By Randolph Fillmore
October 21, 2020

COVID-19 research increasingly reveals how the disease interferes with the body's immune system, and why older people are more vulnerable to its long-term effects. Researchers are also investigating whether COVID-19 permanently impairs the immune system.

A study by Johns Hopkins Medicine researchers published in the September 2, 2020 issue of the journal Blood has begun lighting up the internet and creating plenty of buzz. Now, everyone is asking - "What is factor D and how may knowledge about it help stop COVID-19?"

The study

The study, titled "Direct activation of the alternative complement pathway by SARS-CoV-2 spike proteins is blocked by factor D inhibition," focused on gaining a better understanding of how SARS-CoV-2 attacks the body, causing COVID-19, and ways to stop those attacks.

Thanks to their study, the researchers have some clues. One game changing possibility is that by blocking a protein in the immune system that enables the virus to turn a victim's immune system against itself and start damaging healthy cells, the damaging effects can be subverted.

The Johns Hopkins team concluded that inhibiting the action of a protein, called "factor D," may stop deadly inflammatory reactions many patients have after acquiring the virus. More good news is that there may already be drugs in development and testing that can block factor D.

What is factor D?

None of this is simple as it involves unraveling some of the deeper aspects of the immune system. "Hang on, Ernie. It's going to be a bump-y ride!"

Scientists already know that the spike-like proteins on the surface of the SARS-CoV-2 virus -- making the pathogen look like a golf ball with thorns – allows the molecule to attach to cells targeted for infection. The spikes first grab hold of a substance called "heparan sulfate," a large, complex sugar molecule found on the surface of cells in the lungs, blood vessels and smooth muscle making up most organs. After its initial binding with heparan sulfate, SARS-CoV-2 then uses another cell-surface component, the protein known as "angiotensin-converting enzyme 2" (ACE2), as a "doorway" to get into the cell.

The Johns Hopkins Medicine team found that when SARS-CoV-2 ties up heparan sulfate, it prevents another substance – factor H – from using the sugar molecule to bind with cells. The normal function of factor H is to regulate the chemical signals that trigger inflammation and keep the immune system from harming healthy cells. Without this protection, cells in the lungs, heart, kidneys, and other organs, can be destroyed by the immune system – the very defense mechanism nature intended to safeguard them.

In other words, with factor H functionally dismantled by factor D, the immune system goes crazy and attacks healthy cells. This is also what autoimmune diseases do.

"Previous research has suggested that along with tying up heparan sulfate, SARS-CoV-2 activates a cascading series of biological reactions -- what we call the "alternative pathway of complement" – or APC, that can lead to inflammation and cell destruction of healthy organs if misdirected by the immune system," explained study senior author Robert Brodsky, M.D., director of the hematology division at the Johns Hopkins University School of Medicine. "The goal of our study was to discover how the virus activates this pathway and to find a way to inhibit it before the damage happens."

According to Dr. Brodsky, the APC is one of three chain reaction processes involving the splitting and combining of more than 20 different proteins -- known as complement proteins -- that usually gets activated when bacteria or viruses invade the body. The end product of this complement cascade, a structure called "membrane attack complex" (MAC) forms on the surface of the invader and causes its destruction, either by creating holes in bacterial membranes or by disrupting a virus' outer envelope. However, explained the researchers, MACs also can arise on the membranes of healthy cells. Fortunately, humans have a variety of complement proteins, including factor H, that regulate the APC, keep it in check and protect normal cells from being damaged by MACs.

Is that clear? (Yes, it's complicated. But stay tuned.)

The researchers next used normal human blood serum and three subunits of the SARS-CoV-2 spike protein to discover exactly how the virus activates the APC, then goes on to "hijack" the immune system and endanger normal cells. They found that two of the immune system subunits, called S1 and S2, are the components that bind the virus to heparan sulfate. This binding sets off the APC cascade and blocks factor H from connecting with the sugar, thereby disabling the complement regulation by which factor H keeps the immune response under control.

The immune system's response to chemicals released by killed cells could be responsible for the serious organ damage and organ failures seen in severe cases of COVID-19.

(This is no simple influenza virus!)

The researchers hypothesized that by blocking another complement protein, called "factor D," which works immediately upstream in the pathway from factor H, they could stop the destructive chain of events triggered by SARS-CoV-2. In other words, they used factor D to stop the virus from messing with factor H. It worked. "When we added a small molecule that inhibits the function of factor D, the APC wasn't activated by the virus spike proteins," explained Dr. Brodsky. "We believe that when the SARS-CoV-2 spike proteins bind to heparan sulfate, it triggers an increase in the complement-mediated killing of normal cells because factor H, a key regulator of the APC, can't do its job."

Dr. Brodsky compared this activity to a car in motion…but in trouble.

"If the brakes are disabled, the gas pedal can be floored without restraint, very likely leading to a crash and destruction," he explained. "The viral spike proteins disable the biological brakes, factor H, enabling the gas pedal, factor D, to accelerate the immune system and cause cell, tissue and organ devastation. Inhibit factor D and the brakes can be re-applied and the immune system reset."

Dr. Brodsky added that cell death and organ damage from a misdirected APC associated with factor H suppression is already known to occur in several complement-related human diseases. That includes age-related macular degeneration, a leading cause of vision loss for people age 50 and over and atypical hemolytic uremic syndrome (aHUS), a rare disease that causes blood clots to block blood flow to the kidneys.

Drugs that work like their experiments are already "in the pipeline," said Dr. Brodsky. That means they are under development and/or in clinical trials.

"There are a number of these drugs that will be FDA-approved and in clinical practice within the next two years," said Brodsky "Perhaps one or more of these could be teamed with vaccines to help control the spread of COVID-19 and avoid future viral pandemics."

The other factor D – "The Dive" or, what does it all mean? My take…

What the Johns Hopkins research shows is that COVID-19 induces the immune system into acting against itself, not unlike autoimmune diseases such as rheumatoid arthritis (RA), psoriatic arthritis, multiple sclerosis or, lupus. None of them are known to be caused by a virus, however, and the exact cause of autoimmune disorders is unknown, although some hypothesize that some microorganisms, bacteria or viruses, may trigger changes that "confuse" the immune system and lead to an autoimmune disorder.

According to "Dr. Wikipedia," factor D is a "serine protease that stimulates glucose transport for triglyceride accumulation in fats cells and inhibits lipolysis" (did you get that?) (https://en.wikipedia.org/wiki/Factor_D). The Johns Hopkins research shows that factor D just may be the key to stopping COVID-19's most dangerous, devastating and clandestine function – breaking into cells and hijacking the immune system, enlisting it its most dastardly work -murder.

Colonel Mustard, in the library, with the wrench.

It may be important to note that Dr. Wikipedia adds that "the level of Factor D is decreased in the obese, this reduction may be due to high activity or to resistance, but exact cause is not totally known." Obesity has become one of the better-known risk factors for serious COVID-19 involvement, just ask the former New Jersey governor, Chris Christie. Also, clues that those with already compromised immune systems are especially vulnerable to COVID-19 has been in the spotlight from the beginning.

Dr. Wikipedia goes on to say that "factor D is synthesized by the liver and adipocytes (fat cells) with the latter being the major source." In other words, COVID-19 likes and feeds on fat cells. Factor D has no known natural inhibitors in the body. Most of factor D is eliminated through the kidneys. However, "…in patients with renal disease, factor D was found at elevated levels. The alternative pathway is capable of operating even at low levels of factor D, and deficiencies in levels of factor D are rare."

This means people with kidney disease are quite vulnerable to having their conditions worsen if they contract the virus.

What the "autoimmune-ness" of COVID-19 may also mean is that the "long haul" effects, as they have been called, that is the long-term symptoms and health difficulties associated with having had COVID-19, may not be unlike the long-haul aspects of autoimmune diseases. The question here is whether the immune system is permanently impaired, even in those who are first off asymptomatic? And does this mean that with an impaired immune system, we can expect little to no immunity to the virus? This hint has already been dropped when researchers wonder about people who re-contract COVID-19 after having had it before. They just don't generate enough antibodies, suggesting that their immune systems have been compromised. (More on this farther along, with comments by the expert, Dr. Brodsky)

That older people are particularly vulnerable to COVID-19 makes sense here because the immune system grows weaker with age. Also, that men seem to be more likely than women to die from COVID-19 is a departure from some known aspects of other autoimmune diseases, such as lupus and MS, which are known to strike women more often than men. Some explanations for why women are more prone to autoimmune diseases can be explained by their generally stronger immune systems. Mothers impart part of their immune system to their babies who then, over time build their own immune systems. It may be that stronger immune systems can more easily go haywire, somehow; the weaker the immune system, if one is "immunocompromised," infections can set in more easily.

(For more on this possibility, check out "An Elegant Defense" a book on the immune system that has been both cheered and criticized. See in more resources.)

A final note: TV addicts may be tired of seeing commercials for the array of new drugs that fight the symptoms of autoimmune diseases. Many of these drugs have very pretty commercial names, like "Skyrizi" (risankizumab-rzaa). The scientific names of these drugs all end in "mab," standing for "monoclonal antibody." Monoclonal antibodies are man-made proteins that act like human antibodies in the immune system and are made by cloning a unique white blood cell. All subsequent antibodies derived this way trace back to a unique parent cell. Warnings come with these medications, alerting users to very dangerous, potential side effects, such as developing tuberculosis (TB).

A monoclonal antibody drug with the pharmaceutical name "ravulizumab," and the commercial name of ULTOMIRIS®, is now aimed at COVID-19, as discussed below.

Conclusion

What has been made clearer by this new research is that COVID-19 is truly a monster. It creates its own, temporary, unique autoimmune disease. It is no simple influenza virus wannabe. Those who acquire it can be asymptomatic carriers, or they can be dead, or somewhere in between. That makes COVID-19 an insidious, evil, opportunistic disease that is to be feared. And don't let anyone - anyone - tell you differently.
The hope is that strong and promising research, like that described above, just may be able to stop COVID-19 in its nasty tracks. ▪

A Q&A with Dr. Brodsky

Q - By activating the immune system to essentially attack itself, does that mean that COVID-19 creates its own autoimmune disease? Isn't that far, far different from "normal" influenza virus activity?

A - Yes, in a sense the virus does set off a transient autoimmune or autoinflammatory disease. Once the spike proteins decrease (as the virus clears) complement is no longer unregulated and the process resolves.

Q - Does the hijacking of the immune system this way also relate to what has become called the difficulties of the so-called "long haulers" who – like people with autoimmune diseases – have a lifetime of difficulty?

A - Hard to know. We still don't understand how many people have late effects from COVID-19

Q - Is the drug you are referring to from Alexion Pharmaceuticals, Inc. who are conducting a global Phase 3 study to investigate ULTOMIRIS®(ravulizumab-cwvz)?

A – Yes, Alexion is sponsoring a trial with ravulizumab for COVID-19 patients. Ravulizumab blocks complement downstream of Factor H. In vitro it can block the complement attack triggered by the spike proteins and may be a promising drug therapy. There are several small case series of eculizumab (another C5 inhibitor) being beneficial to patients with COVID-19. However, our data suggest that blocking upstream of factor H, such as with a factor D inhibitor, or a C3 inhibitor, may be an even more effective strategy.

Q - Does this pathway involvement mean that a "simple" vaccine that confers immunity, like a flu vaccine, is not going to be very effective, especially if the immune system is compromised through the "cascade of events"?

A - No. A vaccine will likely be effective if it can prevent the viral load from increasing to the point where complement gets activated. If there are fewer viral particles around, there will be fewer spike proteins to bind heparan sulfate and, hence, less activation of the alternative pathway of complement.

Q - "Doctor Wikipedia" says that "This protein (factor D) is also a serine protease that is secreted by adipocytes into the bloodstream. Finally, the encoded protein has a high level of expression in fat, suggesting a role for adipose tissue in immune system biology…" does that connect to the fact that the obese seem to be at greater risk for poor outcomes of death?

A - Very interesting hypothesis. I can't say for sure but there is no question that obese people have more inflammation, due in part, to complement activation than non-obese patients. How much this is due to factor D levels is unclear. It is also true that heparan sulfate levels on endothelial cells seems to decrease with age and seems to be decreased in pts with the metabolic syndrome; hence, it theoretically would be easier to occupy a great percentage of the heparan sulfate binding sites with less virus in these individuals.

Dr. Brodsky's major clinical research involves the study of aplastic anemia, paroxysmal nocturnal hemoglobinuria and other bone marrow failure disorders. Dr. Brodsky and his colleagues in neurology and rheumatology study severe autoimmune disorders including, scleroderma, myasthenia gravis, multiple sclerosis and autoimmune hematologic disorders.

Other Resources

Johns Hopkins Medicine:
https://www.hopkinsmedicine.org/

Dr. Brodsky bio and research information:
https://www.hopkinsmedicine.org/profiles/results/directory/profile/0007566/robert-brodsky

Clinical trial looks at reducing immune response to help those with serious COVID-19 symptoms:
https://medicine.wustl.edu/news/clinical-trial-focuses-on-reducing-overactive-immune-response-in-covid-19/

An Elegant Defense: The Extraordinary New Science of the Immune System: A Tale in Four Lives, by Matt Richtel
NIH trial of monoclonal antibodies to fight COVID-19:
https://www.nih.gov/news-events/news-releases/clinical-trials-monoclonal-antibodies-prevent-covid-19-now-enrolling

ULTOMIRIS® (ravulizumab-cwvz) now being tested for COVID-19:
https://alexion.com/our-medicines/medicines/ultomiris

Learn more about drugs made with monoclonal antibodies. SKYRIZI (risankizumab-rzaa) (* it is not for COVID-19, but the website is useful for learning about monoclonal antibodies):
https://www.skyrizi.com/about-skyrizi/what-is-skyrizi

About the authors

Stephen A. Smith
Chief storyteller at Consonant Custom Media, healthcare marketing communications professional.

For more than 30 years, Steve's passion has been the strategic management of brands, identity and image. This award-winning creative director has also earned a reputation as an outstanding strategic planner and project manager. Contradiction? Maybe. Perfectionist? Absolutely.

Steve has worked with health systems, brands and nonprofits, including AdventHealth, USF Health, Subaru, Uniroyal and AT&T. He is a member of the Association of Fundraising Professionals (AFP) and the American Hospital Association's Society for Healthcare Strategy and Market Development (SHSMD). The American Advertising Federation, Florida Public Relations Association and International Association of Business Communicators have all recognized his work for creative excellence and effectiveness.

Randolph Fillmore, MA, MA
Science and medical writer, former respiratory therapist and clinical trials coordinator.

With academic training in anthropology and journalism studies, Randy demonstrates an awareness of the "culture" of institutions and organizations, and is able to more fully develop context and capture the "human element" in a story.

Randy has written for university newsletters, websites, magazines, newspapers and reference books. He's also written science features for The Baltimore Sun, the St. Petersburg Times and Stars and Stripes on the topics of genomics, health care issues and policy, medical research, public health, biology, chemistry, environmental sciences, marine science, engineering, physics, pharmacy, and the social sciences.

Mike Eisgrau
Veteran broadcast journalist, native New Yorker with "a face for radio."

Mike received a Masters in Journalism at the Medill Graduate School of Northwestern University. Following a brief flirtation with TV in the heartland, Mike returned to the city he still calls home to polish his skills.

For more than 24 years, Mike could be heard on WNEW 1130 AM, affectionately remembered as "The World's Greatest Radio Station" as a reporter, editor and news director.

Later, Mike served as the director of public affairs at the Jacob K. Javits Convention Center.

Visit with our team of Storytellers here.

What's your perspective?

If the coronavirus pandemic has taught us anything, it's that we are all truly interconnected. At Consonant Custom Media we know that your perspectives matter now more than ever. Make those connections more meaningful by sharing the stories that are woven into the fabric of your organization, its culture and its mission. Strategic storytelling will position you and your team as thought leaders, and magnify your nonprofit mission like nothing else can.

Whether the subject matter is scientific or soul-searching, our brand of content marketing and strategic storytelling – sharing real stories about real people – cuts through the clutter, creates genuine emotional connections and enables a deeper level of engagement. And engagement earns results – in perception management, revenue, relationship building and fundraising.

Support service lines, revenue centers and events. Appeal to the generosity and passion of donors. Reveal the very human side of your medical and support staff. Explain science clearly and concisely. Gain maximum value by repurposing storytelling assets.

Here's what we do:

- Print & Digital Publications
- Editorial & Blogging
- Email Marketing
- Website Design & Content Management
- Video Storytelling
- The Voice Over Studio

To begin the conversation about your content marketing and storytelling, or to view and request samples of our work, visit our website, call us at (941) 309-5380, or send an e-mail.

Consonant
CUSTOM MEDIA

Real Stories. Real Engagement.