Combining Tactical and Strategic Treatments for COVID-19

By

Dr. Ronald N. Kostoff

Research Affiliate, School of Public Policy, Georgia Institute of Technology

Gainesville, VA, 20155

Email: rkostoff@gmail.com

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ABSTRACT

As of mid-March, 2020, many countries in the world are on partial lockdown, to control the spread of the pandemic (COVID-19) resulting from the SARS-CoV-2 coronavirus. The only effective 'treatments' at this time are good hygiene and quarantine. This document presents a novel combined tactical and strategic treatment approach for COVID-19 that incorporates both the tactical and strategic approaches we have developed for preventing and reversing myriad diseases, including treatment repurposing as well. Optimally, the tactical and strategic approach components would be implemented in parallel, to provide benefit from the synergies of the combined approach.

INTRODUCTION

Background

Over the past two decades, there have been at least three major coronavirus-based infectious disease outbreaks/epidemics/pandemics: Severe Acute Respiratory Syndrome (SARS), 2002-2003; Middle East Respiratory Syndrome (MERS), starting in 2012; COVID-19, starting in December 2019. There are a number of similarities among these three infectious diseases, including abnormal values of selected biomarkers (e.g., neutrophils, lymphocytes, albumin, CRP, TNF-alpha, etc), pulmonary inflammation, pulmonary damage, and the demographic affected most severely (elderly, with co-morbidities, and others with weakened immune systems) [1-6].

There are also similarities of COVID-19 with influenza: "Both [COVID-19 and influenza] cause fever, cough, body aches and fatigue; sometimes vomiting and diarrhea; can be mild or severe, even fatal in rare cases; can result in pneumonia" (https://www.hopkinsmedicine.org/health/conditions-and-diseases/coronavirus/coronavirus-disease-2019-vs-the-flu). Additionally, "Neither virus is treatable with antibiotics, which only work on bacterial infections; both are treated by addressing symptoms, such as reducing fever; severe cases may require hospitalization and support such as mechanical ventilation".

One major difference between COVID-19 and influenza is the number of fatalities. According to the above link (and other supporting references), for influenza, the estimate is "1 billion cases worldwide; 9.3 million to 45 million cases in the U.S. ***per year***", accompanied by "291,000 to 646,000 deaths worldwide; 12,000 to 61,000 deaths in the U.S. ***per year***". For the previous coronavirus-based outbreaks/epidemics/pandemics, these cases/fatalities numbers have been orders of magnitude less than the influenza numbers. The SARS pandemic involved about 8,000 people who presented with SARS symptoms, of whom ~800 died [7, 8]. The MERS epidemic involved ~2500 cases, and almost 900 deaths (http://www.emro.who.int/pandemic-epidemic-diseases/mers-cov/mers-situation-update-january-2020.html). As of 21 March 2020, for COVID-19 there are "Approximately 11,906 deaths reported worldwide; 260 deaths in the U.S.", according to the Hopkins link above.

The main measures being taken to control the spread of the SARS-CoV-2 coronavirus (responsible for COVID-19) are conceptually those that were taken to control the spread of the SARS-CoV coronavirus in 2002-2003: good hygiene and quarantine. The difference is the scale of these measures. Currently, many countries are on partial lockdown, restricting many activities and businesses that involve gatherings of large numbers of people in close proximity. It is unknown how long these restrictions will be in place.

Probably the best datapoint on the effectiveness of these stringent measures is that of China, where the current SARS-CoV-2-based infectious disease seems to have started in December 2019. According to Worldometers (https://www.worldometers.info/coronavirus/), which contains country data as well as global data, China has experienced about 75,000 COVID-19 cases and 3300 deaths, as of 21 March 2020. The time curve of China's deaths has essentially ***flattened*** by early-to-mid March, approximately six weeks since the initial rise of cases and deaths. Compare these COVID-19 death statistics in China with those of influenza. According to the following reference (https://championtraveler.com/news/the-us-flu-season-is-bad-this-year-but-influenza-is-still-way-more-deadly-around-the-world/), China averages about 200,000 influenza-associated deaths per year. So, if the China COVID-19 death statistics plot is a true flattening currently, rather than an inflection point, then China's COVID-19-associated deaths (~3300) will be ~1.5% of their average annual influenza-associated deaths (~200,000).

Potential COVID-19 Treatments

Because of uncertainties as to the extent and duration of COVID-19 global spread, myriad treatments are being pursued in parallel. Work on vaccines is being accelerated (https://www.fiercebiotech.com/biotech/biopharma-s-no-holds-barred-fight-to-find-a-covid-19-vaccine-full-list), although widescale implementation is estimated to take perhaps eighteen months or more, assuming positive development results. Treatments being investigated for the interim include potential ***repurposed*** treatments such as remdesivir, chloroquine, hydroxychloroquine, azithromycin, etc (https://techcrunch.com/2020/03/20/hydroxychloroquine-chloroquine-and-other-potential-covid-19-treatments-explained/). These ***repurposed*** treatments are treatments that have been developed for, and applied to, other diseases, and offer the promise of applicability to COVID-19 as well.

Over the past decade+, our research group has been developing protocols for preventing and reversing diseases. These protocols consist of identifying both tactical and strategic treatments (defined in the Methodology section), using different methods to identify these tactical and strategic treatments. In all cases examined, we have identified voluminous amounts of both existing and novel tactical and strategic treatments. In this period of the global COVID-19 crisis, is it possible to integrate our separate treatment identification methodologies into one comprehensive and streamlined approach for both reactively treating COVID-19 in the short-term and proactively strengthening the immune system to reduce susceptibility to similar infections in the long-term? I believe it is, and present the combined approach in the following Methodology section.

METHODOLOGY

Overview

The proposed approach integrates our strategic and tactical treatment approaches. It essentially broadens the tactical treatment approach into covering both prevention and treatment. A summary of the protocol we have developed for preventing and reversing diseases, including potential application to three specific chronic diseases [9-11], is contained in Reference [12]. A recent ***updated*** expansion of our tactical approach used mainly for treatment repurposing, including examples of results from myriad diseases using an ***earlier*** version of the treatment repurposing approach [7, 13-16], is presented in Reference [17].

The proposed integrated approach is as follows. Perform a survey of the relevant literature for the disease of interest (COVID-19, MERS, SARS, etc, in the present case). Identify those biomarkers that show abnormal levels, and identify undesirable symptoms as well. Identify the directions of change desired for the biomarkers and symptoms in order to return to normality. Use this information differently for identifying tactical and strategic treatments, as shown in the following.

Treatment Definition

The details of the crucial step for identifying treatments depend on whether the desired treatment is tactical or strategic, and completing this step fully requires a broadened definition of treatments. If treatments are defined as a set of actions that improve health, then (at least) two types of treatments are possible. The first can be defined as ***positive*** treatments. These are the classical treatments where drugs and/or radiation and/or surgery are implemented, and symptoms are alleviated. These positive treatments are basically a reactive tactical response to abnormal markers of health. They can be applied for the short-term (e.g., antibiotics for bacterial infections, antivirals for viral infections, etc), or for the long-term (e.g., statins, blood thinners, antihypertensives, etc). The second can be defined as ***negative-negative treatments***, where those factors that contribute to disease are first identified and then removed. The name derives from the mathematics world, where a negative of a negative is a positive. These negative-negative treatments are basically a proactive strategic response to abnormal markers of health, and typically involve long-term changes in lifestyle and harmful exposures for improved health.

Tactical Treatments

The proposed approach integrates tactical and strategic treatments. For the tactical treatments, select the most important biomarkers identified, the direction of change desired for each biomarker, and combine these biomarkers and desired directions of change into a query. For example, in the case of COVID-19, assume positive treatment outcomes would result from the following: increase albumin, lymphocytes; decrease CRP, IL-6, IL-1beta [1-6]. Combine these biomarkers and directions of change into a query; there are many ways to do this. One option is a query consisting of all combinations of two biomarkers (e.g., one term in the query might be "increase albumin AND decrease CRP") from the pool of important biomarkers identified. Another option is a query consisting of all combinations of three biomarkers, and so on. Queries actually employed are shown in detail in Reference [17]. If both existing and repurposed tactical treatments are desired, use the query to search all of Medline. For (mainly) tactical treatment repurposing only, search all of Medline except for the core literature that defines the disease of interest (in the present case, the COVID-19, MERS, SARS, etc, literature). The detailed approach to achieve treatment repurposing only is also discussed in Reference [17].

After the query has been entered into the Medline search engine, the retrieved records are examined for existing and/or novel treatments (depending on objectives), and the most promising are selected for further evaluation. Many of the records will contain far more biomarkers and their directions of change than were contained in the query term that retrieved those specific records. For treatment repurposing, one criterion for prioritizing these retrieved candidates is the number of biomarkers in the record that change in the desired directions. Other prioritization criteria are used as well [13-17].

Strategic Treatments

For the strategic treatments, select the important biomarkers identified as above, and the direction of change desired for each biomarker. ***Reverse the desired directions of change***. Combine these biomarkers and new directions of change in a query. For the biomarkers assumed for the COVID-19 case in the previous tactical section, the example query term would now read "***decrease*** albumin AND ***increase*** CRP". If queries with such terms are used to search all of Medline, they would retrieve many records identifying existing and potential ***contributing factors*** to the disease of interest. Once these contributing factors have been identified, their proactive strategic removal would then be recommended. If only novel contributing factors (those not found in the disease core literature) are desired, then, as for the case of repurposed treatments, all of Medline would be searched except for the core literature that defines the disease of interest (in the present case, the COVID-19, MERS, SARS, etc, literature).

Reactive vs Strategic Treatments

The reactive tactical treatment approach for countering infections from viral exposure improves biomarker levels and reduces symptoms (if successful), but ordinarily does little to improve the body's resistance to disease. For viral infections, the tactical treatments will do little to strengthen the weakened immune system. As a result, people with weakened immune systems will again be vulnerable to infection from exposure to the next harmful virus they encounter.

The proactive strategic treatment approach will strengthen the immune (and other) systems by removing those critical factors that contribute to disease and a weakened immune system (unless irreversible damage has been done or individuals have a strong genetic predisposition to disease). These strategic treatments tend to require long-term adherence by their recipients. In turn, these recipients of strategic treatments will be less vulnerable to infection from exposure to the next harmful virus they encounter. Like many healthy people who were exposed to SARS-CoV and SARS-CoV-2, these people who follow the (typically) long-term proactive strategic treatment regimen successfully may not even be aware they have been exposed to the coronavirus. The only indication of their exposure will be coronavirus antibodies in their serum.

CONCLUSIONS AND RECOMMENDATIONS

This document has presented an integrated tactical and strategic treatment approach for COVID-19 in particular, and any infectious disease in general. It is recommended that both the tactical and strategic treatments be implemented in parallel. The tactical treatments might allow the vulnerable to survive the near-term potentially lethal effects of SARS-CoV-2 viral exposure, and the strategic treatments will allow them to be more resistant to future viral attacks of all types.

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ABOUT THE AUTHOR

Ronald Neil Kostoff received a Ph. D. in Aerospace and Mechanical Sciences from Princeton University in 1967. He has worked for Bell Laboratories, Department of Energy, Office of Naval Research, and MITRE Corp. He invented the Wake Shield for producing high vacuum in low orbit, and used in manned space missions for research and development. He has published over 200 peer-reviewed articles, served as Guest Editor of four journal Special Issues since 1994, obtained two text mining system patents, and presently is a Research Affiliate at Georgia Institute of Technology.

He has published on numerous medical topics in the peer-reviewed literature, including:

- potential treatments for
    - Multiple Sclerosis,
    - Parkinson's Disease,
    - Raynaud's Phenomenon,
    - Cataracts,
    - SARS,
    - Vitreous Restoration,
    - Peripheral Neuropathy/Peripheral Arterial Disease
    - Alzheimer's Disease, and
    - Chronic Kidney Disease;
- potential causes of Chronic Kidney Disease;
- potential causes of Alzheimer's Disease;
- potential causes of Peripheral Neuropathy/Peripheral Arterial Disease
- potential impacts of Electromagnetic Fields on health; and
- synergistic effects of toxic stimuli combinations.

His recent publications in toxicology have shown that regulatory exposure limits to toxic stimuli are, on average, orders of magnitude too high compared to exposures shown to cause damage in the biomedical literature, and are not protecting the public from harmful substances.

He is listed in:

- Who's Who in America, 60th Edition (2006),
- Who's Who in Science and Engineering, 9th Edition (2006), and
- 2000 Outstanding Intellectuals of the 21st Century, 4th Edition, (2006).