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I am part of a group of physicians that includes several of the most highly published and well-known critical care experts in the country and world (Drs. Paul Marik, Umberto Meduri, Joseph Varon and José Iglesias).

We have now treated in excess of 100 hospitalized patients with our protocol. Nearly all survived, and the 2 that died were in their eighties and had extensive pre-existing life-threatening conditions. Further, the need for mechanical ventilation has been markedly decreased, and none of our patients has become ventilator dependent nor did they require multiple weeks on a ventilator (a common finding in NYC and Italy). Our patients generally have a short hospital stay and are discharged in good health.

Absence of Effective National and International treatment recommendations.

During the early days of the COVID-19 pandemic, we were quickly dismayed at the collective failure of national and international health societies to recommend any effective treatment protocols for COVID-19. Furthermore, we were alarmed by the increasing emphasis that medical therapies for COVID-19 be tested in prospective, randomized, placebo-controlled trials and that they should only be offered to patients who participated in these clinical trials. This approach ignored the fact that patients with this Coronavirus infection are currently dying of this awful disease and that effective therapeutic approaches likely already exist. We therefore formed the ***Frontline COVID-19 Critical Care Working Group***, a group of world-renowned and highly published Critical Care Experts to deal with this void. If any want to learn more about this group or this treatment protocol, please visit ww.covid19criticalcare.com.

Our group, since the beginning of the pandemic, rapidly and collaboratively reviewed emerging literature from China, Italy and the US, while also systematically gathering the clinical observations and treatment results obtained with various therapeutic strategies from a large group of national and international colleagues. (While in Madison, WI, frantically helping to lead preparations for the expected surge of patients there, I was able to have repeated, daily clinical discussions with many colleagues from multiple New York City area hospitals while they were getting inundated with patients. Please recognize that I am a New Yorker, in fact, I am in NY right now running an ICU full of patients dying of COVID. Anyway, I am blessed to have trained, trained with, and been trained by numerous ICU leaders in New York City, and they comprise a collection of the finest clinicians I know. The time they gave me and the rich clinical conversations we had were invaluable to us. They helped guide and create our insights into what treatments might work.

We developed the MATH+ protocol based on our decades of clinical experience as well as the career research efforts done by members of our group and other leading researchers in the area of organ failure related to severe infections. Our protocol is based on hundreds of peer reviewed medical publications. As a group, we have identified the three core disease processes in COVID-19 and we are simply using three readily available, SAFE and FDA approved medicines to target these disease processes. And the treatment is working.

We've tried to share our protocol and have it adopted for wide-spread use. In fact, we know that it reached the White House for review on at least two, and soon to be three, occasions — the first a month ago via a member of Jared Kushner's COVID response team. We understand that it generated considerable interest and supposedly the N.I.H. and C.D.C. pushed back against it, instead seemingly favoring anti-viral and vaccine therapy. Since then. After an interview that Dr. Marik had with Newt Gingrich on his weekly podcast, Mr. Gingrich asked me and Dr. Marik to write a document outlining the rationale behind the therapy so that he could bring it to the White House for review. Now this week, the editor of the American Spectator, Emmett Tyrrell, after publishing an article about our group and our protocol, asked us to write a letter to President Trump. We do not know if the letter has been delivered, but we still have not heard any response from the White House in response to these efforts.

Our concerns regarding the absence of an effective national treatment strategy intensified after we observed the following:

1) The persistent failure of the currently recommended "supportive care only" strategies — that is, Tylenol and liquids for fever and a ventilator to help them breathe when patients could no longer. This clearly ineffective strategy has led to an unprecedented high mortality and morbidity, while also causing widespread and life-threatening shortages in ventilators, ICU beds, and ICU physicians and nurses.
2) The dissemination of recommendations *against* the use of corticosteroids, which are powerful anti-inflammatory agents, in COVID-19 by the WHO, CDC, ATS, ACP and others. This widespread avoidance of corticosteroid therapy in COVID-19 is, we believe, is a crucial contributor to the high death rate of this disease. My dear colleague, Dr. Umberto Meduri, a member of our group, along with 5 other international world experts in critical care published, 3 weeks ago, in a major medical journal, a review of all studies on corticosteroids therapy in the prior pandemics of SARS, MERS, and H1N1 and concluded, contrary to the medical reviews that informed the WHO and other medical society recommendations, that corticosteroids were life-saving in those prior pandemics in anyone beyond mild illness. Their use led to massive reductions in mortality and the need for ventilators! We are now seeing and hearing about increased use of steroids in an increasing number of centers, however, they are likely still too few and not systematically applied in a protocol.
3) The third alarming factor we have witnessed, many of us firsthand, but also relayed to us by many colleagues, is the increasingly widespread insistence that any proposed medical therapies for COVID-19 only be given to patients who participate in clinical trials. These calls are coming from prominent medical journal editorials and from clinical leadership and "treatment guideline" committees within many leading institutions around the country. We began to hear of increasing "restrictions" against prescribing these well-known and frequently used medications in COVID-19 due to fears that the medicines would "harm " patients. We have also been told about attempts to restrict the ability of physicians to administer these medicines, such as those in our protocol, by describing them as "unproven or experimental" despite the fact they are all FDA-approved medications being used "off label", a practice common to all physicians in myriad disease states.

Let us be clear here: we fully support the need for and execution of clinical trials in COVID-19, however, we want to remind all that trials should **never take precedence over our primary responsibility which is the medical care of our patient.** I want to take a moment to read from the **WORLD MEDICAL ASSOCIATION DECLARATION OF HELSINKI,** which is a statement of ethical

principles for medical research involving human subjects, first formulated in 1964 and last approved in 2013,

1 - The Declaration of Geneva of the WMA binds the physician with the words, "The health of my patient will be my first consideration," and the International Code of Medical Ethics declares that, "A physician shall act in the patient's best interest when providing medical care."

2 - While the primary purpose of medical research is to generate new knowledge, this goal can never take precedence over the rights and interests of individual research subjects.

4. We want to call particular attention to Article 37, which we feel most relevant to delivering medical care in this pandemic: This article is titled: "Unproven Interventions in Clinical Practice"

It reads: "In the treatment of an individual patient, where proven interventions do not exist or other known interventions have been ineffective, the physician, after seeking expert advice, with informed consent from the patient or a legally authorized representative, **may use an unproven intervention if in the physician's judgement it offers hope of saving life, re-establishing health or alleviating suffering.** This intervention should **subsequently** be made the object of research, designed to evaluate its safety and efficacy.

Now I want to focus on what we have proposed as a treatment strategy:

1) First, It is necessary to understand the disease you are treating in order to formulate an effective treatment strategy. In this regard, it soon become evident to us that it is not the virus that is directly killing patients but rather it is the patient's own hyper-inflammatory immune response, which is triggered by the virus, that is leading to progressive organ failure and death. Fundamentally, we need to reduce the "inflammatory storm", early in the course of this disease, **before** irreversible damage (to the lungs) occurs.
2) We have identified the three core disease processes in COVID-19. They are:
    1. Hyper-Inflammation
    2. Hyper-coagulability
    3. Hypoxemia

We are simply using powerful, readily available, FDA-approved medicines with a strong safety profile to target these three processes.

Since we first identified these disease processes, many other centers have also reported similar observations and have proposed similar treatment approaches. We are not claiming to be unique in our treatment approach, but rather that our approach is comprehensive and has an over-riding focus on the timing of initiation. This point cannot be over-emphasized, namely that almost the entire efficacy is dependent on the early delivery of these medicines to the hospitalized patient. Treatment must begin immediately upon the development of low oxygen or respiratory difficulty. This "window for intervention" in COVID-19 appears to be wickedly short and fleeting, requiring hospitals and health care systems to be prepared to implement the protocol, quickly and without hesitation.

Now, the treatments and strategies we propose are explained below:

Front Line Covid-19 Critical Care Working Group "MATH+" PROTOCOL:

All three medicines must be started within 6 hours of admission to the hospital:

1) **METHYLPREDNISONE –** a powerful anti-inflammatory drug that we use to suppress the immune system and prevent organ damage. COVID-19 is causing a condition called the "cytokine storm" for which this drug, a corticosteroid, is the standard recommended treatment accepted around the world.
2) **ASCORBIC ACID–** although known as Vitamin C, when delivered intravenously, this substance acts as a powerful "stress hormone" that controls inflammation and prevents the development of leaky bloody vessels in the lung, thus avoiding the development of lung failure which is the condition causing death in almost all COVID-19 patients.
3) **HEPARIN -** COVID-19 is causing widespread blood clotting, preventing blood flow to vital organs such as the brain, lungs, and extremities. Heparin is a blood thinner which prevents the formation of these blood clots and thus preserves blood flow to these vital organs. We recommend the subcutaneous form of heparin, called enoxaparin, which has a long safety record and is easy for nurses to administer.
4) **OXYGEN SUPPORT** – In addition to the 3 medications listed above, we have found that maximizing the use of a high-flow nasal oxygen delivery devices allows the avoidance of invasive mechanical ventilation, which itself damages the lungs and is associated with a mortality rate approaching nearly 90% in some centers.

Several of our ***Frontline COVID-19 Critical Care Working Group*** have seen firsthand how this simple treatment protocol can reduce the devastating complications of this disease and return patients to a quality of life that they value.

I want to call attention to a more recent concerning development: based on the experiences during the first surge of patients, which overwhelmed many hospitals in NYC and Seattle, horror stories describing weeks on mechanical ventilators leading to the death of nearly all patients, these reports have ***created a second catastrophe — the now widespread reluctance of patients to seek care in the hospital. Consequently, many new cases are arriving in hospitals in the more advanced phase of the illness, with often irreversible organ failure (lung) that poorly respond to any treatment protocol, even ours.*** We must place all focus on immediately reeducating the population and physicians alike. They must know that an effective treatment strategy exists, but that it only works if initiated ***early*** in the course of COVID-19.

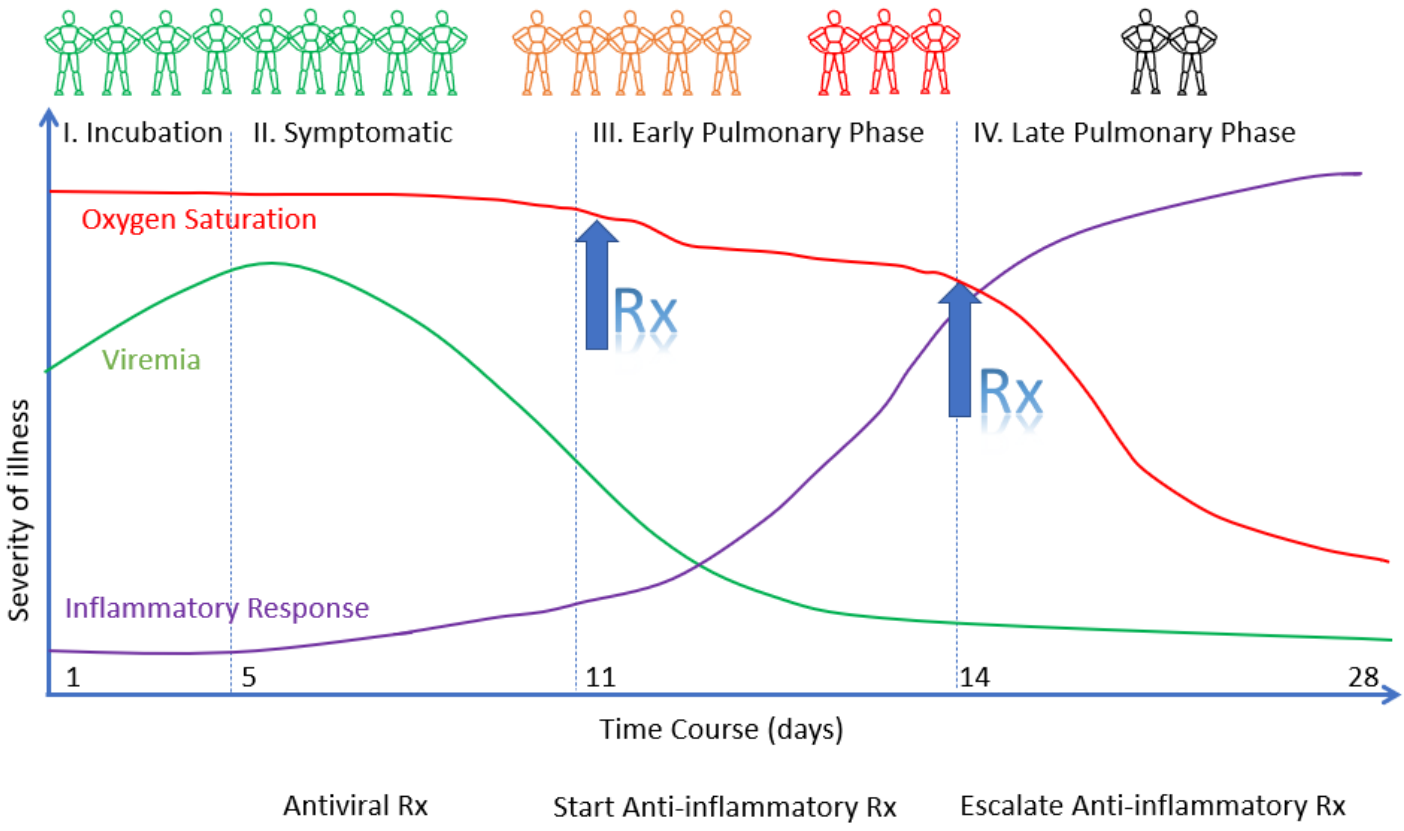
As for the timing:

Figure 1 below, illustrates the importance of understanding the two distinct, yet overlapping, phases of this disease.

1. <u>The viral replicative phase</u> — this occurs early, largely in outpatients. Mild symptoms: fevers, fatigue, body aches, and sore throat are felt as the virus directly invades the tissues and causes systemic symptoms (but no organ dysfunction)
    i. This is the phase anti-viral therapies should be focused on, i.e. before patients reach the hospital where medicines like hydroxychloroquine or Remdesivir would have the greatest impact to keep the patient away from the hospital and ICU

2. <u>The hyper-inflammatory, immune response phase</u> (what brings patient to the hospital) is a state of immune system dysregulation whereby immune cells exit the blood vessels into tissues, causing massive inflammation within and failures of the major organs, most commonly the lungs, brain, heart, and kidneys.

It is this later, hospitalized "hyper-inflammatory" phase that our protocol is designed to treat and where experts in hospital and ICU medicine are needed.



If you have time, I'd like to share with you a couple of **Facebook posts that have come in to us over the past 2 weeks.**

“We floundered for two weeks. Lots of codes, intubations and death. Maybe 15 discharges. We started steroids and discharge 250 patients. Less intubations, less codes. And the ones that ended up on vent, not as serious. CXR/CT Changes = steroids Hypoxia on admission = steroids Ambulatory hypoxia = steroids Completely changed our trajectory Steroids are a game changer” Hospitalist, SE Michigan - our group is taking care of 700 plus COVID+ patients

John DP –

“I'm here in New Orleans and we've been using it for the last four weeks. We notice a great success once we started using steroids. Do not underestimate this study. This was a game changer in our hospital. We were able to free ventilators and get elderly patients out of the hospital without needing a ventilator. Patients that were obviously crushing quickly, who we had to have end of life talk with were able to walk out of the hospital. At no point did any of our patient worsen and because of steroids. These patients shed viruses 4 weeks later, With or without steroids. The virus doesn't kill anybody, it’s the inflammation that does. Let the virus replicate however slow down the inflammation”

Before I conclude, I also want to bring attention to this report from the Henry Ford Health System in Detroit, whereby a company named Advaita Bioinformatics, analyzed data from the medical records of COVID-19 patients within that system, and they are now reporting that Methyprednisolone use, the drug which is the mainstay of our protocol, even in a short course, led to less ICU transfers, less need for ventilators, and less mortality. See this link for the full report https://engineering.wayne.edu/news/wayne-state-spinoff-advaita-bioinformatics-identifies-generic-drug-shown-to-be-effective-against-covid-19-39569

SUMMARY/CONCLUSION

Our protocol has been out over 4 weeks. It is not unique, in fact, we are not alone in what we propose or have been trying — as you can read in the experiences posted above by doctors. In fact, we are seeing an increasing number of similar protocols with nearly identical therapeutics come out from various institutions and countries, including the Italian guidelines, Chinese Guidelines, Yale protocol, Montefiore protocol and others.

We are doctors, trained to diagnose and treat illness, we are experts in our field with decades of experience and hundreds of publications. However, we most pride ourselves by the skills we have gained at the bedside in caring for patients. We have clearly devised an effective treatment for use, prior to the publication of randomized controlled trials. Those trials are critical for sure, as they will help us further refine and/or perfect our treatment doses, durations, and indications, but waiting for the **perfect** is and will be the enemy of the **good,** which we are already achieving and will continue to achieve for many. We just want to save lives, and we know how to do it.