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I want to start by saying that I am part of a group of physicians which include 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). In response to the COVID crisis we formed the Front-Line Critical Care Working group, our protocol can be found at covid19criticalcare.com

Members of our group have now treated in excess of 100 hospitalized patients with our treatment protocol. Nearly all survived, The 2 that died were in their eighties and had advanced chronic medical conditions. None of the patients have had long stays on the ventilator nor become ventilator dependent. The patients generally have a short hospital stay and are discharged in good health.

Absence of Effective National and International treatment recommendations.

Before I go into the process and rationale for our treatment protocol, I want to highlight three critical factors that we feel are contributing to the COVID-19 crisis which we call upon the health societies to address:

- 1) The fact that nearly all national and international health societies such as the WHO, CDC, ACP, ATS, and many others have issued treatment recommendations focusing almost solely on “supportive care only” strategies, things like Tylenol for fever, gentle hydration/nutrition then oxygen or a ventilator to support breathing.. This strategy is clearly failing as evidenced by unprecedented death rates and widespread and life-threatening shortages in ventilators, ICU beds, and ICU physicians and nurses. Our early recognition of the failure of this treatment approach is what prompted us to form our group
- 1) The 2nd factor is these same health societies dissemination of recommendations *against* the use of corticosteroids in COVID-19. We want to immediately call the worlds attention to this tragic error, based on the following emerging data:
 - a. A senior member of our group, and an international expert in corticosteroid therapy in critical illness, Dr. Umberto Meduri, along with 5 other international critical care experts published, 3 weeks ago, a comprehensive analysis of corticosteroid therapy during the prior pandemics of SARS, MERS, and H1N1 and their analysis found, contrary to the WHO recommendations, that corticosteroids were life-saving in those prior pandemics when given to anyone beyond mild illness.
 - b. Sorin Draghici, CEO of Advaita Bioinformatics just reported that their incredibly sophisticated Artificial Intelligence platform called iPathwayGuide, using cultured human cell lines infected with COVID-19 is able to map all the human genes which are activated by this virus, as they have done for other viruses such as influenza. Note almost all the activated genes are those that express triggers of inflammation. With this knowledge of the specific COVID inflammatory gene activation combined with knowledge of the gene suppression activity of all known medicines they were able to match the most effective drug for COVID-19 human gene suppression.. and that drug is methylprednisolone (this must be recognized, as the ability of other corticosteroids to control inflammation in COVID-19 was much less impactful. This is, we believe, an absolutely critical and historic finding. Many centers are using similar but less effective agents such as dexamethasone or prednisone..

2) 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>

- a. Around the same time of this discovery, Dr. Mayur Ramesh, an Infectious disease specialist and Immunologist at Henry Ford Hospital rapidly performed a study of methylprednisolone therapy in over 200 COVID-19 patients and they found that early methylprednisolone reduced LOS, ventilator needs and mortality
- b. Finally, in a study that is currently under review from a group of Spanish critical care experts that we are in contact with, they found that an early and longer course of methylprednisolone therapy led to a massive reduction in mortality
- c. Now, let me read some reports posted on Facebook by some anonymous doctors in Michigan:
“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 , since we started using steroids, We were able to free ventilators and get elderly patients out of the hospital without needing a ventilator. Patients that were obviously crashing 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 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”

- 3) The third alarming factor we have witnessed, many of us firsthand, is the increasingly widespread insistence within institution, medical journals, and health societies that any proposed medical therapies for COVID-19 only be given to patients who participate in clinical trials. We are aware of instances whereby “restrictions” were proposed and placed against commonly used FDA approved medicines if used off-label in COVID-19, a practice that all doctors do every day.

Our group also supports the need for and execution of clinical trials in COVID-19, however, we want to remind everyone in regards to medical research in this pandemic that

1 - The Declaration of Geneva of the WMA binds the physician with the words, “The health of my patient will be my first consideration,”

2- International Code of Medical Ethics declares that, “A physician shall act in the patient’s best interest when providing medical care.”

3- Article 37 of the WMA declaration of Helsinki, titled: “[Unproven Interventions in Clinical Practice](#)”

It reads, and I paraphrase: “In the treatment of an individual patient, where proven interventions do not exist, a physician **may use an unproven intervention if in the physician’s judgement it offers hope of saving life, re-establishing health or alleviating suffering.**”

In response to these three factors, Our group 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. One of my main contributions to this effort came from my large network of

ICU colleagues in NYC where I trained, trained with, and was trained by many NYC ICU leaders. Basically, From the early days when I was in Madison, WI frantically helping lead preparations for the expected surge of patients to now where I am running an ICU in NYC full of dying COVID patients, many in their 2nd to 3rd week on ventilators with end-stage fibrotic lung disease, I was able to have repeated, daily clinical discussions with ICU leaders from multiple New York City area hospitals The time they gave me and the rich clinical conversations we had were invaluable to us.

Based on these clinical impressions, an exhaustive review of the early literature, our decades of clinical experience as well as the career research by members of our group we identified the three core disease processes in COVID-19 and then collaboratively developed our MATH+ protocol. This protocol is based on hundreds of peer reviewed medical publications and uses three readily available, SAFE and FDA approved medicines to target these disease processes. And the treatment is working.

The three core pathologic processes in COVID-19 are:

- 1) Hyper-Inflammation-
- 2) Hyper-coagulability
- 3) Hypoxemia

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.

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. **Having treated patients in NYC for the past two weeks, it is my very strong insight that** This “window for intervention” in COVID-19 appears to be wickedly short and fleeting, it will require all the hospitals and health care systems to be prepared to implement the protocol, quickly and without hesitation

I am seeing treatment fail here in NYC for a frightening reason – namely that based on the experiences

during the first surge of patients which overwhelmed many hospitals in NYC and led to horror stories of shortages in critical staff, ventilators, medicines and beds with all associated with patients spending weeks on mechanical ventilators leading to the death of most, 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.

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.

Finally, we want it to be known that with the support of several physician colleagues and members of the media, we have tried to share our protocol widely. 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 until supposedly the N.I.H. and C.D.C. pushed back against it, instead seemingly favoring antiviral and vaccine therapy. Later, Dr. Paul Marik was interviewed by former Speaker 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. Still no response. 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 hope it gets to him.

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.

As for the timing:

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

1. The viral replicative phase — 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. The hyper-inflammatory, immune response phase (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.

