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support@Covid19CriticalCare.com

The MATH+ Protocol Is Showing Profound Impacts on Survival of COVID-19 Patients

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Months ago, early on in COVID-19, the FLCCC created the **MATH+** protocol based on their insights into COVID-19 as a steroid-responsive disease. This treatment recommendation went against all the major national and international health care societies that had mis-interpreted the medical literature, a body of published evidence which, upon careful and deep review actually supported the use of corticosteroids in prior pandemics. One of our members, Dr. G. Umberto Meduri, published the landmark paper which highlighted the errors the societies had made in recommending against the use of corticosteroids, and despite it being published in a journal of the Society of Critical Care Medicine, which then disseminated it to all of its members, little systemic change in treatment approaches occurred. Thousands of patients who became critically ill with COVID-19 and who were suffering from massive inflammation may have been saved if this safe and powerful anti-inflammatory medicine had been provided.

We would like to call attention to the news of a major, large, randomized controlled trial which validates our now long-standing recommendation that corticosteroids must be used, and be used early on, in the hospital course of a COVID-19 patient. The RECOVERY trial, conducted by the University of Oxford, reported today that the use of a corticosteroid called dexamethasone improved survival by 1/3 in ventilated

patients and by a 1/5 in patients requiring oxygen. While news of these impacts is deeply encouraging and validates our months-long position that COVID-19 is indeed a steroid-responsive disease, **we believe that larger and more dramatic impacts on survival can be achieved with the drug and dosing strategy incorporated into MATH+**.

The reasons for this are as follows: 1) Methylprednisolone reaches high concentrations in lung tissue and 2) Based on analysis of the inflammatory gene activation patterns induced by SARS-CoV-2, Methylprednisolone gene suppression activity most closely matches it, suggesting a higher efficacy when used in COVID-19 than dexamethasone and 3) The dose of dexamethasone in the RECOVERY trial was modest and likely insufficient for more severe cases. The Methylprednisolone dose advocated by the FLCCC has been shown to be the most highly effective dose based on prior pandemics and ARDS trials. Additionally, the FLCCC advocates for longer durations as well as escalation/tapering according to the clinical

condition of each individual patient. A prospective Italian study using this protocol was submitted for publication and the results will be disclosed upon acceptance.In the hospitals of two of our FLCCC physicians—each having treated over 100 hospitalized patients with **MATH+** often early on in the hospitalization, the hospital mortality rate to date is **6.6%** in one hospital (Dr. Paul Marik, Norfolk, VA) and less than **3.3%** in the other (Dr. Joseph Varon, Houston, TX). Manuscripts are in progress.

The **MATH+** protocol was developed using the deep clinical expertise of these highly published Critical Care medicine physician-scholars. We believe that **MATH+** saves lives. And, if implemented widely, it will save thousands.

*The medical community is aggressively conducting many research studies in an attempt to find treatments for patients being admitted to hospitals with low oxygen levels or who are struggling to breathe. Given that these trials may take months or years to produce actionable guidance, as a working group with over two hundred years of combined experience in Critical Care and Emergency Medicine, we designed the **MATH+** COVID-19 Early Intervention Treatment Protocol and, to date, are having remarkable success using it to treat patients in hospitals that permit its use. We are in the process of gathering patient data to scientifically prove its efficacy.*

The administration of intravenous methylprednisolone and ascorbic acid along with the anticoagulant heparin, starting in the emergency room and continued until recovery, has led to large reductions in the the mortality rate of this disease and the need for mechanical ventilation. Anticoagulation is used to counteract the high rates of life-threatening blood clots caused by the excessive amount of inflammation caused by COVID-19.

Our team includes clinician scholars with the highest level of bedside expertise and more than 1,500 articles published in peer-reviewed journals, including many in the areas of corticosteroid and intravenous ascorbic acid use in critical illness, sepsis, and acute respiratory distress syndrome (ARDS).

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MATH+
HOSPITAL TREATMENT PROTOCOL FOR COVID-19

MATH+ **v5**
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TO CONTROL INFLAMMATION & EXCESS CLOTTING

In all COVID-19 hospitalized patients, the therapeutic focus must be placed on early intervention utilizing powerful, evidence-based therapies to counteract:

— The overwhelming and damaging inflammatory response
— The systemic and severe hyper-coagulable state causing organ damage

By initiating the protocol soon after a patient meets criteria for oxygen supplementation, the need for mechanical ventilators and ICU beds will decrease dramatically.

MATH+ PROTOCOL

[Only for use in hospitals in the treatment of COVID-19]

1. **Methylprednisolone** [Intravenous]
   — A. Mild hypoxia (< 4L): 40 mg daily until off oxygen
   — B. Moderate-severe illness: 80 mg bolus, then 20mg q6h IV push for 7 days*
      • Alternate: 40 mg q12h for 7 days*
   — Day 8: Switch to oral prednisone, taper over 6 days

   *Consider higher doses for patients with non-improving ARDS/oxygenation and/or with persistent, rising, or severely elevated inflammatory markers (cytokine storm), i.e. 60–125 mg q6h–q8h, or 1,000 mg/day for 3 days

2. **Ascorbic Acid** [High Dose Infusion]
   — 3 grams / 100 ml q6h
   — Continue for a total of 7 days or until discharged

3. **Thiamine**
   — 200 mg IV q12h until discharged

q6h/q12h = every 6/12 hours
1 mg Heparin = 500 int. units (IU)
CrCl = Creatinine Clearance (C_{Cr})

4. **Heparin** [Low Molecular Weight Heparin / LMWH]
   — A. Stable patient on medical floor/ward: 0.5 mg/kg q12h; if CrCl ≤ 30 ml/min, give once a day
   — B. Critically ill or ICU patient: 1 mg/kg q12h unless contraindicated, dose adjust for CrCl 15–30 ml/min
      • If CrCl ≤ 15 ml/min, use unfractionated heparin [UFH]
      • Monitor antifactor-Xa activity, target range is 0.6–1.1 units/ml
   — Continue until discharged

5. **PLUS** optional co-interventions: Melatonin (6–12 mg at night), Zinc (75–100 mg/day), Vitamin D3 (2,000–4,000 units/day), Statin (Atorvastatin 40–80 mg/day preferred), Famotidine (40 mg/day), and Magnesium (2 g IV in ICU patients only, target Mg level between 2.0–2.4 mmol/l).

TREATMENT OF LOW OXYGEN

— If patient has low oxygen saturation on nasal cannula, initiate heated high flow nasal cannula.
— Do not hesitate to increase flow limits as needed.
— Avoid early intubation that is based solely on oxygen requirements. Allow "permissive hypoxemia" as tolerated.
— Intubate only if patient demonstrates excessive work of breathing.
— Utilize "prone positioning" to help improve oxygen saturation.

For updates, references and more information please see

www.covid19criticalcare.com | www.flccc.net

MATH+
HOSPITAL TREATMENT PROTOCOL FOR COVID-19

ABOUT THE MATH+ HOSPITAL TREATMENT PROTOCOL FOR COVID-19

Our **MATH+** protocol is designed for hospitalized patients, to counter the body's overwhelming inflammatory response to the SARS-CoV-2 virus. The protocol is based on numerous medical journal publications over decades. It is the hyper-inflammation, not the virus itself, that damages the lungs and other organs and ultimately causes death in COVID-19. We have found the **MATH+** protocol to be a highly effective combination therapy in controlling this extreme inflammatory response.

The steroid **M**ethylprednisolone is a key component, increasing numbers of studies (see https://flccc.net/medical-evidence) show its profound effectiveness in COVID-19, which is made more potent when administered intravenously with high doses of the antioxidant **A**scorbic acid given that the two medicines have multiple synergistic physiologic effects. **T**hiamine is given to optimize cellular oxygen utilization and energy consumption, protecting the heart, brain, and immune system. The anticoagulant **H**eparin is important for preventing and dissolving blood clots that appear with a very high frequency in patients not given blood thinners. The **+** sign indicates several important co-interventions that have strong physiologic rationale and an excellent safety profile. It also indicates that we plan to adapt the protocol as our insights and the published medical evidence evolve.

Timing is a critical factor in the successful treatment of COVID-19. Patients must go to the hospital as soon as they experience difficulty breathing or have a low oxygen level. The **MATH+** protocol then should be administered soon after a patient meets criteria for oxygen supplementation (within the first hours after arrival in the hospital), in order to achieve maximal efficacy as delayed therapy has led to complications such as the need for mechanical ventilation.

If administered early, this formula of FDA-approved, safe, inexpensive, and readily available drugs can eliminate the need for ICU beds and mechanical ventilators and return patients to health.

DISCLAIMER

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