

The Fleming [FMTVDM] Directed CoVid-19 Treatment Protocol.

¹Richard M. Fleming, PhD, MD, JD (ORCID 0000-0001-9964-1518)

¹Matthew R. Fleming, BS, NRP

¹FHHI-OI-The Camelot Foundation
Los Angeles, CA, USA

Running title: The Fleming [FMTVDM] Directed CoVid-19 Treatment Protocol.

Address all correspondence to:
Richard M. Fleming, PhD, MD, JD
DrRichardMFleming@gmail.com

Key words: Fleming, FMTVDM, CoVid-19 Pneumonia (CVP)

Protocol Date: 15 April 2020*

*CLINICAL TRIALS.GOV IDENTIFIER: *NCT04349410*

PROTOCOL MODIFICATION 4 JULY 2020 TO BE FOLLOWED AND PLACED IN APPENDIX G.

TABLE OF CONTENTS.....	i-ii
ABSTRACT	1
FMTVDM DIRECTED CoVID-19 PNEUMONIA (CVP) TREATMENT PROTOCOL.....	1-17
SIMPLIFIED EXPLANATION OF FMTVDM.....	2-3
FMTVDM CoVID-19 PNEUMONIA TREATMENT PROTOCOL.....	3-14
A. PROPOSED AEROSOLIZED AND INTRAVENOUS ADMINISTRATION OF ALL POSSIBLE MEDICATIONS.....	3-4
B. PROPOSED TREATMENT REGIMENS. [TREATMENT CONSISTS OF THREE COMPONENTS: (1) ONE OF THE 10 TREATMENTS LISTED BELOW, (2) THE IMMUNE SUPPORTIVE TREATMENT, AND (3) ATROVENT NEBULIZER TREATMENTS.].....	5-8
TREATMENT COMPONENT ONE.....	5-7
TREATMENT COMPONENT TWO.....	7
TREATMENT COMPONENT THREE.....	8
VENTILATOR SETTINGS.....	8
C. FMTVDM MEASUREMENT OF THE EXTENT OF DISEASE AND DETERMINATION OF TREATMENT RESPONSE.....	8-9
D. SEQUENCE OF FMTVDM TESTING THROUGH CoVID-19 DIAGNOSIS & TREATMENT...9-10	
FMTVDM MEASURED OUTCOMES OF TREATMENT.....	10
SCENARIO 1: IMPROVEMENT.....	10
SCENARIO 2: DETERIORATION.....	10
SCENARIO 3: NO CHANGE.....	10
SUMMARY OF FMTVDM PATENT RIGHTS #9566037.....	10-11
SUMMARY OF THE TREATMENT PROTOCOLS FOR CoVID-19.....	12
REFERENCES.....	13-14
TABLE 1. CHARACTERISTICS OF DIAGNOSTIC IMAGING.....	15
FIGURE 1. FMTVDM QUANTITATIVE MEASUREMENT ALONG THE HEALTH-SPECTRUM.....	16

FIGURES 2. FMTVDM QUANTIFICATION OF PULMONARY TISSUE.....17-18

APPENDIX A. FMTVDM CALIBRATION AND IMAGING PROTOCOLS.....19-34

 STEP 1A: CALIBRATION OF PLANAR AND SPECT/CT SYSTEMS.....20-23

 STEP 1B: CALIBRATION OF PET SYSTEMS.....24-26

 STEP 2A: FMTVDM PLANAR OR SPECT/CT IMAGING PROTOCOL.....27

 STEP 2B: FMTVDM PET IMAGING PROTOCOL.....28-29

 STEP 3: PATIENT COVID-19 FMTVDM MEASUREMENT AND MEANING OF RESULTS.....30-34

 STEP 4: DELIVERY OF RESULTS TO NUCLEAR MEDICINE, PATIENT CHART & DR FLEMING...34

APPENDIX B. TABLES FOR COLLECTING, RECORDING AND CALCULATING CAMERA CALIBRATION.....35-43

 APPENDIX B1: FOR PLANAR AND SPECT/CT FMTVDM QUANTITATIVE CALIBRATION.....36-39

 APPENDIX B2: FOR PET FMTVDM QUANTITATIVE CALIBRATION.....40-43

APPENDIX C. FMTVDM INDIVIDUAL PATIENT DATA FORMS.....44-53

 FMTVDM PLANAR OR SPECT/CT REPORT FORM.....46-49

 FMTVDM PET REPORT FORM.....50-53

APPENDIX D. CUMULATIVE INDIVIDUAL PATIENT SERIAL FMTVDM PATIENT DATA.....54-57

APPENDIX E. SCHEMATIC OF FINAL PROTOCOL SEQUENCE.....58-59

APPENDIX F. FLEMING UNIFIED THEORY OF VASCULAR DISEASE (THE INFLAMMATION AND HEART DISEASE THEORY) EXPLAINS CRS & INCREASED BLOOD CLOTTING.....60-65

APPENDIX G. FLEMING FMTVDM TREATMENT PROTOCOL EFFECTIVE 4 JULY 2020.....66-67

ABSTRACT

Diagnostic determination of disease and treatment responses has been limited to qualitative imaging, measurement of serum markers of disease, and sampling of tissue. In each of these instances, there is a built in error either due to sensitivity and specificity issues, clinician interpretation of results, or acceptance of the use of an indirect marker (blood test) of what is happening elsewhere in the body – at the tissue level.

*The Fleming Method for Tissue and Vascular Differentiation and Metabolism (FMTVDM) using same state single or sequential quantification comparisons [1] provides the first and only patented test (#9566037) - along with the associated submitted patent applications ruled to be covered under #9566037 - that quantitatively measures changes in tissue resulting from *inter alia* a disease process. This includes *inter alia* coronary artery disease (CAD), cancer and infectious/inflammatory processes including CoVid-19 pneumonia (CVP) resulting from the metabolic and regional blood flow differences (RBFs) caused by these diseases.*

The purpose of this paper is to make clinicians and researchers aware of this proposed method for investigating the prevalence and severity of CVP - in addition to providing rapid determination of treatment response in each patient, directing treatment decisions; thereby reducing the loss of time, money, resources and patient lives.

FMTVDM Directed CoVid-19 Pneumonia (CVP) Treatment Protocol

The major reason for fear and panic is the absence of a treatment that works for CoVid-19 pneumonia.

We don't know what works because we have no treatment information.

Everyone is scrambling to propose their ideas but the proposed studies have nothing to demonstrate treatment outcomes short of patients living or dying. We need to define outcomes long before that.

By this we specifically mean, there is no proposal for showing what these treatments are doing at the tissue level - the lungs - during treatment and absent this information we are left with clinical changes only.

FMTVDM is the only patented method, which can quantitatively measure where the patient is and the result of their treatment.

SIMPLIFIED EXPLANATION OF FMTVDM [1].

FMTVDM quantitatively measures changes in tissue – including inflammatory and infectious states and place people on a continuum [2] as shown in Figure 1. The critical differences between qualitative, semi-quantitative and quantitative FMTVDM are shown in Table 1 [2]. Examples of measurements taken in both pulmonary and cardiac tissue are shown in Figure 2.

FMTVDM [1-6] – See Appendix A.

1) Quantitatively calibrates the nuclear camera to guarantee that the measurements made by the camera are accurate, consistent and reproducible. This quantification is dependent upon the isotope being used, the camera and the timing sequence of image acquisition. Such calibration is NOT currently done and it is part of the patent. Studies have demonstrated that the *lack of this quantitative calibration* has resulted in up to 1/3 of the data being lost for SUV and qualitative interpretation; in addition to making quantification impossible [6].

2) The patient presents in a fasting state - to eliminate digestive processes from interfering with blood flow distributions - and the differences in metabolic and regional blood flow differences (RBFs) are enhanced with vasodilatory agents, shifting blood flow and isotope towards regions of greater blood flow and metabolism; enhancing isotope delivery, uptake and quantification.

3) With a now quantitatively calibrated nuclear camera – in this instance a PLANAR camera – or SPECT/CT or PET/CT/MRI if specifically approved¹ - to allow imaging to be done at patient's bedside reducing the use of hospital resources required for transport and decrease potential for patient complications resulting from a transport - image acquisition will occur for 10-minutes following peak enhancement effect of the vasodilatory agent and timed injection of the isotope based upon the enhancing agent.

Regions-of-interest (ROIs) will drawn by the nuclear technologist – either at the bedside or in the nuclear laboratory – to provide FMTVDM measurements using software already present in the nuclear camera systems. Specific ROIs will be drawn of the right lung (total), left lung (total), mediastinum (thymus activity), and any specific areas where increased tracer uptake is noted [7].

4) These FMTVDM measurements including **MAXIMAL COUNTS +/- VARIANCE**, provide the values of the most active pulmonary tissue resulting from the CoVid-19 infection and inflammatory response; just as it has previously been used for CAD and Cancer.

5) From these FMTVDM measurements, the pulmonary tissue and the CoVid-19 infectious process results are placed on a Health-Spectrum showing where in the

¹ Specific details including imaging times and quantification change as noted in the protocol.

tissue transitioning process the patient is [2]. The measurements also provide information about how rapidly the tissue is changing [1]. FMTVDM provides the quantitative measurement of where the patient is at any point in time during their course of treatment and how they compare with other patients.

6) Once the FMTVDM measurements have been obtained, treatment decisions can be made based upon serial changes in FMTVDM. Treatments outcomes are based upon FMTVDM measurements, including the maximum FMTVDM and the variance in those measurements [1]. By comparing serial FMTVDM results, improvement or deterioration in the patient's health and the success or failure of the current treatment regimen is measured, providing patient-centered, patient-specific, patient-oriented and patient-directed decisions. Thus saving time, money, resources and lives - not to mention unnecessary side effects from treatment, which is not working.

I. FMTVDM CoVID-19 PNEUMONIA TREATMENT PROTOCOL:

Patients who screen positive by PCR who require admission to the hospital will undergo FMTVDM testing immediately prior to initiation of treatment. If patients have already initiated treatment, FMTVDM will be useful to assess the status of the patient moving forward.

Following FMTVDM treatment will be started and patients will undergo standard monitoring and supportive care in addition to the selection of the following treatment options noted below.

A. PROPOSED AEROSOLIZED AND INTRAVENOUS ADMINISTRATION OF ALL POSSIBLE MEDICATIONS.

In 2001, anthrax terrorism, introduced multiple people to a bacillus (*Bacillus anthracis*), which had endospores. The physicians who successfully treated their patients did so by recognizing they were dealing with an endospore species of bacterial. The combined medical treatment of ciprofloxacin, doxycycline and clindamycin – to varying degrees – proved effective because they targeted a specific component of the bacillus; the endospore.

It is clear that the medications, which have been proposed for treating CoVid-19 pneumonia – *inter alia* chloroquine, hydroxychloroquine, remdesivir – target the specific features of transcription and translation; obvious viral targets.

When the first author was an Intern, he helped treat the oldest known living cystic fibrosis patient. The patient came to the hospital every 6-8 weeks and required antibiotic treatment. That treatment was an experimental aerosolized ciprofloxacin. Only by delivering the ciprofloxacin directly into his lungs, was the antibiotic able to achieve satisfactory tissue levels to address his pneumonia.

The lungs of CoVid-19 patients appear to exhibit the same type of significant reductions in function as our cystic fibrosis patient. Resulting both from localized pneumonia (CVP) and associated acute respiratory distress syndrome (ARDS) resulting from this inflammatory process [3,7].

Azithromycin, one of the proposed treatments, which like all macrolide antibiotics, works by inhibiting ribosomal translation of protein synthesis. **Azithromycin is available in the aerosolized form.**

*Each and every medication delivered for the purpose of treating the CoVid-19 virus patient should be delivered via **aerosol** to obtain maximum pulmonary tissue penetration. Those drugs, which cannot be given by aerosol, should be given **intravenously** when possible; with **oral** delivery being the final alternative for giving medications, which cannot be delivered by aerosol or intravenous administration.*

Also in keeping with the first author's training during his internship year, when he rotated on the Oncology service with Dr. Hankensen; is the principal that seriously ill patients do not spontaneously get better and timely responses to data is necessary to improve patient outcomes and reduce morbidity and mortality. For patients with cancer, who "spiked" a fever and demonstrated a bacterial infection, patients automatically underwent testing (applicable blood and other tests) to look for the source and agent of infection. Patients were simultaneously started in gram-positive and gram-negative coverage. If patients did not improve within 36-48 hours, a macrolide antibiotic was added. If no improvement was noted within 36-48 hours, an antifungal agent was initiated followed by antiviral therapy if no improvement was noted in the next 36-48 hours. Once the organism was identified, treatment was tailored back to the offending organism.

CoVid-19 Pneumonia (CVP) and inflammation is no less serious and in many ways more so. Given the morbidity and mortality associated with CoVid-19, the treatment and diagnostic evaluation with FMTVDM, takes this same aggressive treatment approach.

B. PROPOSED TREATMENT REGIMENS. [TREATMENT CONSISTS OF THREE COMPONENTS: (1) ONE OF THE 10 TREATMENTS LISTED BELOW, (2) THE IMMUNE SUPPORTIVE TREATMENT, AND (3) ATROVENT NEBULIZER TREATMENTS.]

Since we do NOT YET know which medical regimen² will be the most effective, it is our recommendation that each facility make a selection of treatments and randomly assigns patients to treatment groups. The following treatments are recommended based upon the information we currently have available.

TREATMENT COMPONENT ONE^{3 4}

Treatment 1: Hydroxychloroquine 200 mg po q 8 hrs (600 mg qD) for a total of 10-days, and Azithromycin 500 mg IV on day 1, followed by 250 mg IV on days 2-5 (to prevent bacterial superinfection⁵).

Treatment 2: Hydroxychloroquine 200 mg po q 8 hrs (600 mg qD) for a total of 10-days, and Doxycycline 100mg IV q 12 hrs with each dose given over 1 to 4-hours (to prevent bacterial superinfection⁶).

Treatment 3: Hydroxychloroquine 200 mg po q 8 hrs (600 mg qD) for a total of 10-days. Clindamycin⁷ 150-450 mg po q6 hours x 10 days OR 4800 mg IV daily – beginning with 150 mg initial rapid infusion, followed by continuous infusion q 24-hours for 7-days.

To maintain serum clindamycin levels	Rapid infusion rate	Maintenance infusion rate
Above 4 mcg/mL	10 mg/min for 30 min	0.75 mg/min
Above 5 mcg/mL	15 mg/min for 30 min	1.00 mg/min
Above 6 mcg/mL	20 mg/min for 30 min	1.25 mg/min

² All routine blood testing and observations for potential treatment side effects must be observed.

³ **The dosages shown are for adult patients. Pediatric and adolescent dosage should be adjusted accordingly.**

⁴ **FOR ANY PATIENT WITH QTc GREATER THAN 500 msec, or for which there is clinician concern for rhythm disturbance, β 1 blockers such as ATENOLOL OR ESMOLOL SHOULD BE USED TO REDUCE CONCERNS FOR PROLONGED QTc DYSRHYTHMIAS.**

⁵ And to inhibit ribosomal protein synthesis (translation) of CoVid-19.

⁶ And to inhibit ribosomal protein synthesis (translation) of CoVid-19.

⁷ Binding to 50S ribosomal subunit interfering with protein translation of virus.

Treatment 4⁸: Hydroxychloroquine 200 mg po q 8 hrs (600 mg qD) for a total of 10-days. Primaquine⁹ 200 mg po on day # 1. Clindamycin¹⁰ 150-450 mg po q6 hours x 10 days OR 4800 mg IV daily – beginning with 150 mg initial rapid infusion, followed by continuous infusion q 24-hours for 7-days.

To maintain serum clindamycin levels	Rapid infusion rate	Maintenance infusion rate
Above 4 mcg/mL	10 mg/min for 30 min	0.75 mg/min
Above 5 mcg/mL	15 mg/min for 30 min	1.00 mg/min
Above 6 mcg/mL	20 mg/min for 30 min	1.25 mg/min

Treatment 5¹¹: Hydroxychloroquine Day # 1: 800 mg po initially followed by 400 mg 8 hours later. Days 2 and 3: 400 mg po qD. Primaquine¹² 200 mg po on day # 1. Clindamycin¹³ 150-450 mg po q6 hours x 10 days OR 4800 mg IV daily – beginning with 150 mg initial rapid infusion, followed by continuous infusion q 24-hours for 7-days.

To maintain serum clindamycin levels	Rapid infusion rate	Maintenance infusion rate
Above 4 mcg/mL	10 mg/min for 30 min	0.75 mg/min
Above 5 mcg/mL	15 mg/min for 30 min	1.00 mg/min
Above 6 mcg/mL	20 mg/min for 30 min	1.25 mg/min

Treatment 6: Remdesivir 200 mg IV on day 1, followed by 100 mg IV qD for a total of 10-days.

Treatment 7: Tocilizumab¹⁴ 8mg/kg IV (not to exceed 800 mg) over 60-minutes. If clinical improvement is not noted, three additional doses may be administered at q 8-hour intervals from the initial infusion for a total of 4-doses maximum. ANY PATIENT DEMONSTRATING CYTOKINE RELEASE SYNDROME WILL HAVE THIS TREATMENT ARM AUTOMATICALLY ADDED.

⁸ Treatments 4 and 5 are based upon malarial regimens previously used and shown to be effective in malarial eradication.

⁹ Primaquine should not be given to G6PD deficiency patients.

¹⁰ Binding to 50S ribosomal subunit interfering with protein translation of virus.

¹¹ Treatments 4 and 5 are based upon malarial regimens previously used and shown to be effective in malarial eradication.

¹² Primaquine should not be given to G6PD deficiency patients.

¹³ Binding to 50S ribosomal subunit interfering with protein translation of virus.

¹⁴ Monoclonal antibody inhibiting IL-6. Prescribed dosage regimen for Cytokine Release Syndrome (CRS) – aka Cytokine Storm.

Treatment 8: Methylprednisolone 80 mg IV over 30-minutes, BID x 7-days. Then taper off.

Treatment 9: Interferon alpha-2b 5 million units per nebulizer BID.

Treatment 10: Losartan 25 mg po qD.

Treatment 11: Plasma transfusions from CoVid-19 survivors.

Treatment 12: Further treatments will be added or deleted based upon further information, diagnostic outcomes or information we receive from you.

Each patient should also have daily homocysteine (Hcy)¹⁵ levels checked. Elevations in Hcy are an indirect serum marker of a failed immune system as noted in the original “Inflammation and Heart Disease” Theory and measured treatment responses of bacterial infections aggravating CAD [3,7]. Electrocardiograms should also be obtained to monitor QTc intervals, as well as potassium and magnesium levels if QTc prolonged – for possible electrolyte replacement.

Caution should be applied to the amount of blood taken from patients for diagnostic comparison testing – remembering and taking into account the minimum amount of blood needed from each patient for each test - and not simply filling vacutainer tubes of blood.

TREATMENT COMPONENT TWO

The following additional immune supportive treatment should be added to the above treatment regimens, focusing on immune function.

Folate 3 mg qD, Magnesium 400 mg qD,
Calcium Carbonate 400 mg qD, Vitamin B12 - 3 mg qD,
Vitamin B6 - 30 mg qD, DHEA 50 mg BID,
Vitamin C 2000 mg qD, Zinc 10 mg po or 4 mg IV¹⁶, and
Vitamin D3 1500 IU qD.

¹⁵ Patients should have **daily labs** including CBC with differential, CRP, LFT’s, renal function – a metabolic panel should include all renal, liver tests and electrolytes – and a serum ferritin for possible cytokine release syndrome. A daily nasal and/or oral PCR swab should be obtained to obtain comparison data of possible changes in this screening test and to compare with FMTVDM and clinical response.

¹⁶ When possible Zinc should be given IV.

TREATMENT COMPONENT THREE¹⁷

To improve/enhance airway exchange of O₂/CO₂ and delivery of any nebulized Rx.

Atrovent¹⁸ (β₂ bronchodilator) nebulizer treatments q 4-hours.

VENTILATOR SETTINGS

VENTILATOR SETTINGS¹⁹ FOR PATIENTS WITH ARDS SHOULD BE SET AT 5-6 ML/KG BODY WT, WITH ADJUSTMENTS TO KEEP PEAK PLATEAU PRESSURE AT NO MORE THAN 30 CM H₂). PRONE POSITIONING SHOULD BE CONSIDERED.

By keeping track of the treatment response of patients using FMTVDM measurements, changes in medication regimens should focus on those showing the best FMTVDM treatment outcomes.

Treatment recommendations from the 12 – targeted treatment options [additional targeted treatment options may be added] should be randomized so we can learn rapidly, what works and what doesn't, with changes in treatment based upon what is working in other patients and other hospitals.

C. FMTVDM MEASUREMENT OF THE EXTENT OF DISEASE AND DETERMINATION OF TREATMENT RESPONSE.

PLANAR BEDSIDE: Upon presentation a FMTVDM test will be conducted pursuant to FMTVDM patent including (a) quantitative calibration of the nuclear camera – preferably a portable planar²⁰ camera to reduce transportation of patients (which would require additional personnel, problems with ventilatory assistance, etc), (b) enhancement to shift blood flow and isotope to areas with greater regional blood flow and metabolism followed by FMTVDM imaging and measurement²¹, (c) nuclear technologist drawn regions-of-interest (ROIs) for quantification as described above, (d) FMTVDM measurements, including entire right and left lung fields, thymus region and

¹⁷ Improved exchange of O₂/CO₂ and ability to decrease tidal volumes – reducing further inflammatory changes within pulmonary tissue including ARDS.

¹⁸ β₂ bronchodilator without cardiac effect enhancing airway function and O₂/CO₂ exchange.

¹⁹ **Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. N Engl J Med 2000;342(18):1301-1308.**

²⁰ **LEHR collimator with initial setting of 128 x 128 matrix, with settings changed based upon Quantitative Calibration of camera as explained in Appendix A & B. It is not unexpected that following the initial calibration, that a change in matrix to 64 x 64 will be needed to address missed scintillated decay emissions.**

²¹ Lantheus isotopes and products are excluded from the study.

all areas of visually apparent isolated isotope uptake. FMTVDM values will include maximum values +/- variance.

NUCLEAR LABORATORY: For patients that are either not ventilated OR for those facilities which have established the protocol and dedicated nuclear camera for infectious patients – including CoVid-19 patients, imaging options include SPECT²², SPECT/CT, SPECT/MRI, PET, PET/CT or PET/MRI.

The calibration and imaging sequence of the anatomic component (CT or MRI) of the RMTVDM study, should – at least for the present time – follow the currently used imaging standards established at each facility for each camera.

The quantitative calibration of the PLANAR, SPECT and PET components of these cameras for FMTVDM imaging and quantification are detailed in Appendices A and B.

D. SEQUENCE OF FMTVDM TESTING THROUGH COVID-19 DIAGNOSIS & TREATMENT.

Patients will undergo treatment for 48-72 hours, based upon clinical status and staffing availability. The outcomes will be based upon measured changes in maximum +/- variance of FMTVDM values. [An increase in variance demonstrates changing pulmonary conditions while a smaller variance demonstrates consistency of tissue change. When coupled with the maximal FMTVDM measurements, variance provides information about the transitional changes occurring.]

²² SPECT = single photon emission computed tomography; PET = positron emission tomography.

FMTVDM MEASURED OUTCOMES OF TREATMENT

SCENARIO 1: Patients demonstrate **improvement** after 48 to 72-hours of treatment.

FMTVDM has been repeated and the quantified results of tissue change compared with the initial/prior study shows reductions in maximum FMTVDM numbers. If the results show improvement, then patients should remain on the regimen. FMTVDM should be repeated 3 to 7-days later to compare further tissue response to treatment and reassess further treatment.

SCENARIO 2: Patients clinically **deteriorates** after 48 to 72-hours of treatment – or sooner if clinically indicated.

FMTVDM numbers increase compared with the prior FMTVDM study. Treatment should be immediately changed – either randomly assigning another treatment from the above options OR selecting treatment which FMTVDM has shown to be beneficial in other patients - with another FMTVDM to be done 48 to 72-hours following this change in treatment to assess new treatment effect.

SCENARIO 3: Patients demonstrate **no change** on FMTVDM compared with the prior study after 48 to 72-hours of treatment..

Based upon these results, patient's treatment will either (a) remain the same (based upon clinical signs), or (b) be modified (including additional drugs) - if the clinician believes there has been no improvement clinically or is concerned with clinical deterioration. Following this treatment decision, another FMTVDM should be completed 48 to 72-hours later to reassess treatment response.

SUMMARY OF FMTVDM PATENT RIGHTS - #9566037 [1].

The publication of a proposed study is both an unusual practice for the authors and the journal - particularly when it includes the incorporation of intellectual property.

As a routine, clinical research studies remain closely guarded secrets with information only released following completion of the study. However, these are not routine times. A pandemic has swept across the globe impacting almost every country in the world. The mortality rate associated with CoVid-19 is greater than anything seen in our lifetimes. It is overwhelming our medical systems, our economies and our peoples.

Consequently, the primary author realizes that the dissemination of his intellectual property could be compromised by those choosing to take advantage of the information provided - but that is a concern, which must be addressed another day. Truly, the needs of the many, outweigh the needs of the few, or the one. In this

instance the first author is willing to take the chance that people will do the right thing as we share this information through the journal.

Dr. Fleming will for the duration of this pandemic, following a signed NDA - either by the FDA to cover everyone, or from each institution - and explanation with each center further specific details on how FMTVDM is to be done, allow FMTVDM to be done on CoVid-19 patients waiving any licensing fees or royalties for this study and the treatment of these critically ill people.

SUMMARY OF THE TREATMENT PROTOCOLS FOR COVID-19²³

	Treatment 1	Treatment 2	Treatment 3	Treatment 4	Treatment 5	Treatment 6	Treatment 7	Treatment 8	Treatment 9	Treatment 10	Treatment 11	Treatment 12
IMMUNE SUPPORT: Folate 3 mg qD, Magnesium 400 mg qD, Calcium Carbonate 400 mg qD, Vitamin B12 - 3 mg qD, Vitamin B6 - 30 mg qD, DHEA 50 mg BID, Vitamin C 2000 mg qD, Zinc 10 mg po or 4 mg IV, and Vitamin D3 1500 IU qD. RESPIRATORY SUPPORT: Atrovent (β2 bronchodilator) nebulizer treatments q 4-hours.	X	X	X	X	X	X	X	X	X	X	X	X
❖ COVID-19 TARGETED TREATMENTS												
Hydroxychloroquine 200 mg po q 8 hrs (600 mg qD) for a total of 10-days	X	X	X	X								
Azithromycin 500 mg IV on day 1, followed by 250 mg IV on days 2-5	X											
Doxycycline 100mg IV q 12 hrs with each dose given over 1 to 4-hours		X										
Clindamycin 150-450 mg po q6 hours x 10 days OR 4800 mg IV daily – beginning with 150 mg initial rapid infusion, followed by continuous infusion q 24-hours for 7-days			X	X	X							
Primaquine 200 mg po on day # 1.				X	X							
Hydroxychloroquine Day # 1: 800 mg po initially followed by 400 mg 8 hours later. Days 2 and 3: 400 mg po qD.					X							
Remdesivir 200 mg IV on day 1, followed by 100 mg IV qD for a total of 10-days.						X						
Tocilizumab 8mg/kg IV (not to exceed 800 mg) over 60-minutes. If clinical improvement is not noted, three additional doses may be administered at q 8-hour intervals from the initial infusion for a total of 4-doses maximum.							X					
Methylprednisolone 80 mg IV over 30-minutes, BID x 7-days. Then taper off.								X				
Interferon alpha-2b 5 million units per nebulizer BID.									X			
Losartan 25 mg po qD.										X		
Plasma transfusions from CoVid-19 survivors.											X	

²³ If the patient experiences Cytokine Release Syndrome (CRS) – Cytokine Storm – **Tocilizumab** is to be **added** immediately to the current treatment protocol **OR IF THE FMTVDM RESULTS SHOW ACTIVATION OF THE THYMUS GLAND.**

FMTVDM MEASUREMENT REFERENCES

1. The Fleming Method for Tissue and Vascular Differentiation and Metabolism (FMTVDM) using same state single or sequential quantification comparisons. Patent Number 9566037. Issued 02/14/2017.
2. Fleming RM, Fleming MR, Dooley WC, Chaudhuri TK. Invited Editorial. The Importance of Differentiating Between Qualitative, Semi-Quantitative and Quantitative Imaging – Close Only Counts in Horseshoes. *Eur J Nucl Med Mol Imaging*. 2020;47(4):753-755. DOI:10.1007/s00259-019-04668-y. Published online 17 January 2020 <https://link.springer.com/article/10.1007/s00259-019-04668-y> <https://rdcu.be/b22Dd>
3. Fleming RM. Chapter 64. The Pathogenesis of Vascular Disease. Textbook of Angiology. John C. Chang Editor, Springer-Verlag New York, NY. 1999, pp. 787-798. doi:10.1007/978-1-4612-1190-7_64.
4. Fleming RM, Harrington GM, Baqir R. Heart Disease in Men. Chapter 3. *Using Multiple Images Post-Stress to Enhance diagnostic Accuracy of Myocardial Perfusion Imaging: The Clinical Importance of Determining Washin and Washout Indicates a Parabolic Function between Coronary Perfusion (Blood Flow) and Cellular ("Uptake/Release") Function*. Alice B. Todd and Margo H. Mosley Editors, Nova Publishers, 2009, pp. 75-100. (https://www.novapublishers.com/catalog/product_info.php?products_id=8409)
5. Fleming RM, Harrington GM, Baqir R, Jay S, Challapalli S, Avery K, Green J. Renewed Application of an Old Method Improves Detection of Coronary Ischemia. A Higher Standard of Care. *Federal Practitioner* 2010;27:22-31.
6. Fleming RM, Harrington GM. Chapter 13. Fleming Harrington Redistribution Wash-in Washout (FHRWW): The Platinum Standard for Nuclear Cardiology. *Establishing Better Standards of Care in Doppler Echocardiography, Computed Tomography and Nuclear Cardiology*. Richard M. Fleming, Editor, Intech Publishing July 2011. ISBN: 978-953-307-366-8. DOI:10.5772/22369.
7. Fleming RM. The Fleming Unified Theory of Vascular Disease: A Link Between Atherosclerosis, Inflammation, and Bacterially Aggravated Atherosclerosis (BAA). *Angiol* 2000; 51: 87-89.

TREATMENT REFERENCES

1. Touret F, de Lamballerie X. Commentary Of Chloroquine and VOVID-19. *Antiviral Research* 2020;177:104762. doi:10.1016/j.antiviral.2020.104762.
2. Colson P, Rolain J-M, Lagier J-C, Brouqui P, Raoult D. Chloroquine and hydroxychloroquine as available weapons to fight COVID-19. *International Journal of Antimicrobial Agents* (2020), doi: <https://doi.org/10.1016/j.ijantimicag.2020.105932>

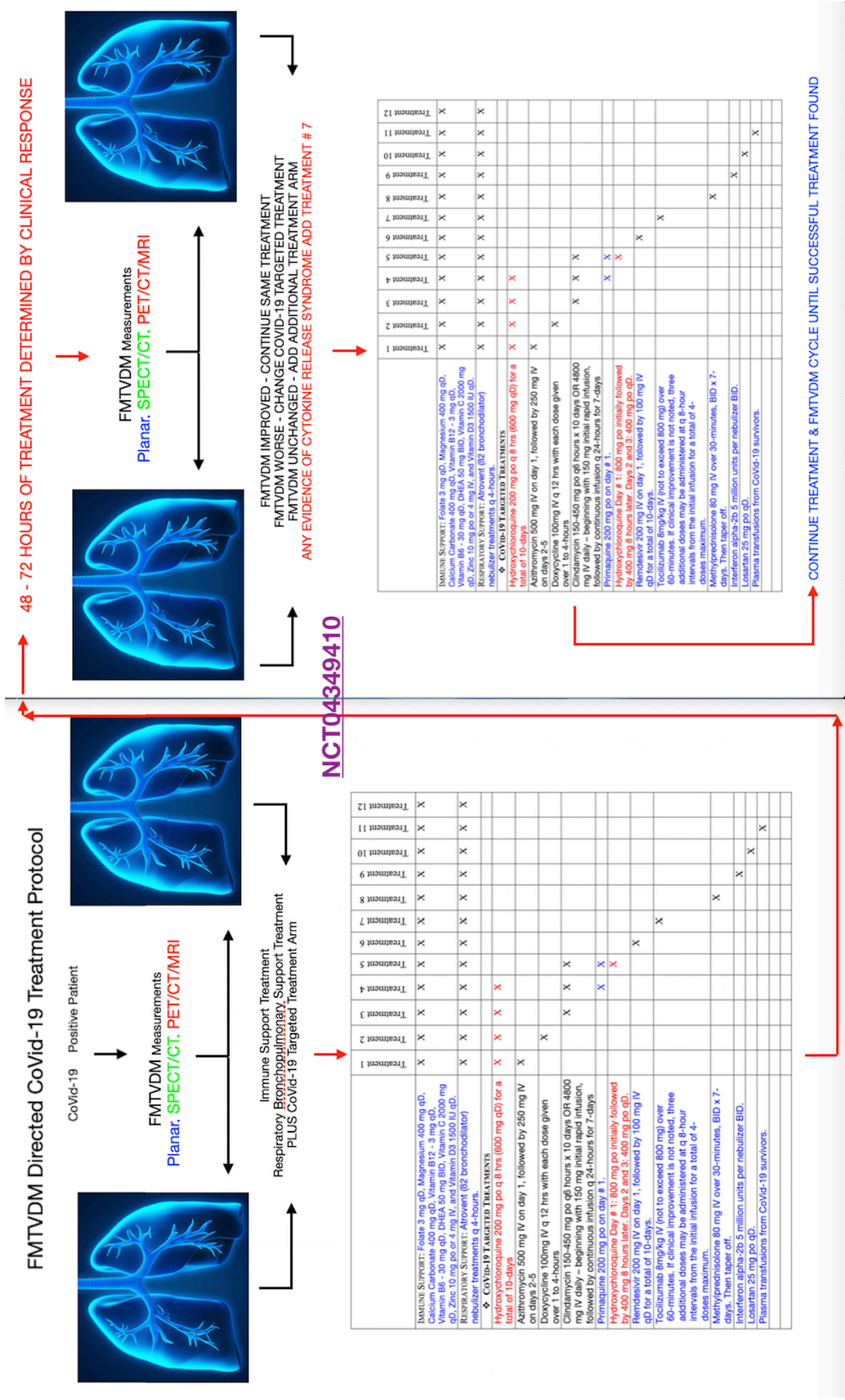
3. Padberg S. Anti-infective Agents. 2015. Elsevier B.V. Drugs During Pregnancy and Lactation. <http://dx.doi.org/10.1016/B978-0-12-408078-2.00007-X>
4. 8-Aminoquinoline – an overview. Science Direct Topics. 8-Aminoquinoline - an overview | Science Direct Topics.html
5. Gautret P, Lagier J-C, Parola P, et al. Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial. medRxiv preprint doi: <https://doi.org/10.1101/2020.03.16.20037135>.
6. Santarpia JL, Rivera DN, Herrera V, et al. Transmission Potential of SARS-CoV-2 in Viral Shedding Observed at the University of Nebraska Medical Center. medRxiv preprint doi: <https://doi.org/10.1101/2020.03.23.20039446>.
7. Cheng VCC, Lau SKP, Woo PCY, Wu R. Severe Acute Respiratory Syndrome Coronavirus as an Emerging and Reemerging Infection. Clinical Microbiology Reviews Oct. 2007:660-694.
8. Wu Ruo, Lin S-y, Zhao H-m. Albuterol in the treatment of acute respiratory distress syndrome: A meta-analysis of randomized controlled trials. World J Emerg Med 2015;6(3):165-171.
9. Arpaia N, Barton GM. Toll-like Receptors: Key Players in Antiviral Immunity. Curr Opin Virol 2011;1(6):447-454.
10. Bhatraju PK, Ghassemieh BJ, Nichols M, et al. Covid-19 in Critically Ill Patients in the Seattle Region – Case Series. N Engl J Med 2020. DOI: 10.1056/NEJMoa2004500.
11. Med QLM, Guan X, Wu P, et al. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus – Infected Pneumonia. N Engl J Med 2020;382(13):1199-1207.
12. Haston JC, Hwang J, Tan KR. Guidance for Using Tafenoquine for Prevention and Antirelapse Therapy for Malaria – United States, 2019. MMWR 2019;68(46):1062-1068.
13. Shen C, Wang Z, Zhao F, et al. Treatment of 5 Critically Ill Patients With COVID-19 With Convalescent Plasma JAMA 2020. Published online March 27, 2020. E1-E8.
14. Gautret P, Lagier J-C, Parola P, et al. Clinical and microbiological effect of a combination of hydroxychloroquine and azithromycin in 80 COVID-19 patients with at least a six-day follow up: an observational study. Prepublication galley. April 2020.
15. Zheng F, Liao C, Fan Q-h, et al. Clinical Characteristics of Children with Coronavirus Disease 2019 in Hubei, China. Current Medical Science 2020;40(2):1-6.
16. Recht J, Ashley E, and White N. Safety of 8-Aminoquinoline Antimalarial Medicines. WHO 2014. ISBN 978 92 4 150697 7.
17. Chen C, Gao G, Xu Y, et al. SARS-CoV-2-Positive Sputum and Feces After Conversion of Pharyngeal Samples in Patients With COVID-19. Annals of Internal Medicine. Published 30 March 2020:1-3.

TABLE

Table 1. Characteristics distinguishing three approaches to diagnostic imaging [2].

	Qualitative imaging	Semi-quantitative	Quantitative
Results discussed in scientific literature	Sensitivity and specificity errors	Sensitivity and specificity errors	Accurate, consistent, reproducible
Calibration	Camera not quantitatively calibrated. Interpretation per human eye	Camera not quantitatively calibrated. Estimates against something not actually measured by the imaging device	Camera <i>IS</i> quantitatively calibrated. Calibrated to that which the camera actually measures —scintillation emissions
Reported as	Normal, mild, moderate, severe, absent	Ratios: Derived from <i>time per injected radiation per patient body weight or Radiation per gram per volume</i>	Absolute value: Emissions measured and quantitatively compared with radioactive decay of isotope
Interpretation	Subjective	Subjective with various assumptions	Objective
Application to artificial intelligence	Not applicable given errors in sensitivity and specificity	Not applicable given errors in sensitivity and specificity	Already incorporated into machine-to-machine (M2M)—AI

Table Legend: The use of anatomic tests like radiographs, computed tomography (CT), currently employed single photon emission computed tomography (SPECT), planar (stationary SPECT), positron emission tomography (PET) without standard uptake values (SUV), ultrasound, and tests providing anatomic data are qualitative. Tests such as coronary artery calcium (CAC) and PET with SUV's are semi-quantitative using a series of assumptions. FMTVDM provides the only truly quantitative method for measuring tissue changes



Treatment	Treatment 1	Treatment 2	Treatment 3	Treatment 4	Treatment 5	Treatment 6	Treatment 7	Treatment 8	Treatment 9	Treatment 10	Treatment 11	Treatment 12
IMMUNE SUPPORT: Folate 3 mg qd, Magnesium 400 mg qd, Calcium Carbonate 400 mg qd, Vitamin B12 - 3 mg qd, Vitamin B6 - 30 mg qd, DHEA 50 mg BID, Vitamin C 2000 mg qd, Zinc 10 mg po or 4 mg IV, and Vitamin D3 1500 IU qd.	X	X	X	X	X	X	X	X	X	X	X	X
RESPIRATORY SUPPORT: Astrotent (B2 bronchodilator) nebulizer treatments q 4-hours.	X	X	X	X	X	X	X	X	X	X	X	X
COVID-19 TARGETED TREATMENTS	X	X	X	X	X	X	X	X	X	X	X	X
Hydroxychloroquine 200 mg po q 8 hrs (600 mg qd) for a total of 10-days	X	X	X	X	X	X	X	X	X	X	X	X
Azithromycin 500 mg IV on day 1, followed by 250 mg IV on days 2-5	X	X	X	X	X	X	X	X	X	X	X	X
Doxycycline 100mg IV q 12 hrs with each dose given over 1 to 4-hours	X	X	X	X	X	X	X	X	X	X	X	X
Clofazimine 150-450 mg po qd hours x 10 days OR 4800 mg IV daily - beginning with 150 mg initial rapid infusion, followed by continuous infusion q 24-hours for 7-days	X	X	X	X	X	X	X	X	X	X	X	X
Primaquine 200 mg po on day # 1	X	X	X	X	X	X	X	X	X	X	X	X
Hydroxychloroquine Day # 1: 800 mg po initially followed by 400 mg 8 hours later. Days 2 and 3: 400 mg po qd for a total of 10-days.	X	X	X	X	X	X	X	X	X	X	X	X
Remdesivir 200 mg IV on day 1, followed by 100 mg IV qd for a total of 10-days.	X	X	X	X	X	X	X	X	X	X	X	X
Tocilizumab 8mg/kg IV (not to exceed 800 mg) over 90-minutes. If clinical improvement is not noted, three additional doses may be administered at 8-hour intervals from the initial infusion for a total of 4-doses maximum.	X	X	X	X	X	X	X	X	X	X	X	X
Methylprednisolone 80 mg IV over 30-minutes, BID x 7-days. Then taper off.	X	X	X	X	X	X	X	X	X	X	X	X
Interferon alpha-2b 5 million units per nebulizer BID. Losartan 25 mg po qd.	X	X	X	X	X	X	X	X	X	X	X	X
Plasma transfusions from CoVID-19 survivors.	X	X	X	X	X	X	X	X	X	X	X	X