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

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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 (RBFDs) 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 (RBFDs) 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 approved[1] - 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 regimen[2] 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 superinfection[5]).

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 superinfection[6]).

Treatment 3: Hydroxychloroquine 200 mg po q 8 hrs (600 mg qD) for a total of 10-days. Clindamycin[7] 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, ß1 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 4[8]: Hydroxychloroquine 200 mg po q 8 hrs (600 mg qD) for a total of 10-days. Primaquine[9] 200 mg po on day # 1. Clindamycin[10] 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 5[11]: Hydroxychloroquine Day # 1: 800 mg po initially followed by 400 mg 8 hours later. Days 2 and 3: 400 mg po qD. Primaquine[12] 200 mg po on day # 1. Clindamycin[13] 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: Tocilizumab[14] 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 IV[16], 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 THREE[17]

To improve/enhance airway exchange of 02/CO2 and delivery of any nebulized Rx.

Atrovent[18] (ß2 bronchodilator) nebulizer treatments q 4-hours.

VENTILATOR SETTINGS

VENTILATOR SETTINGS[19] 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 planar[20] 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 measurement[21], (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] ß2 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 SPECT[22], 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 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-19[23]

	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: Atrovent (ß2 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.

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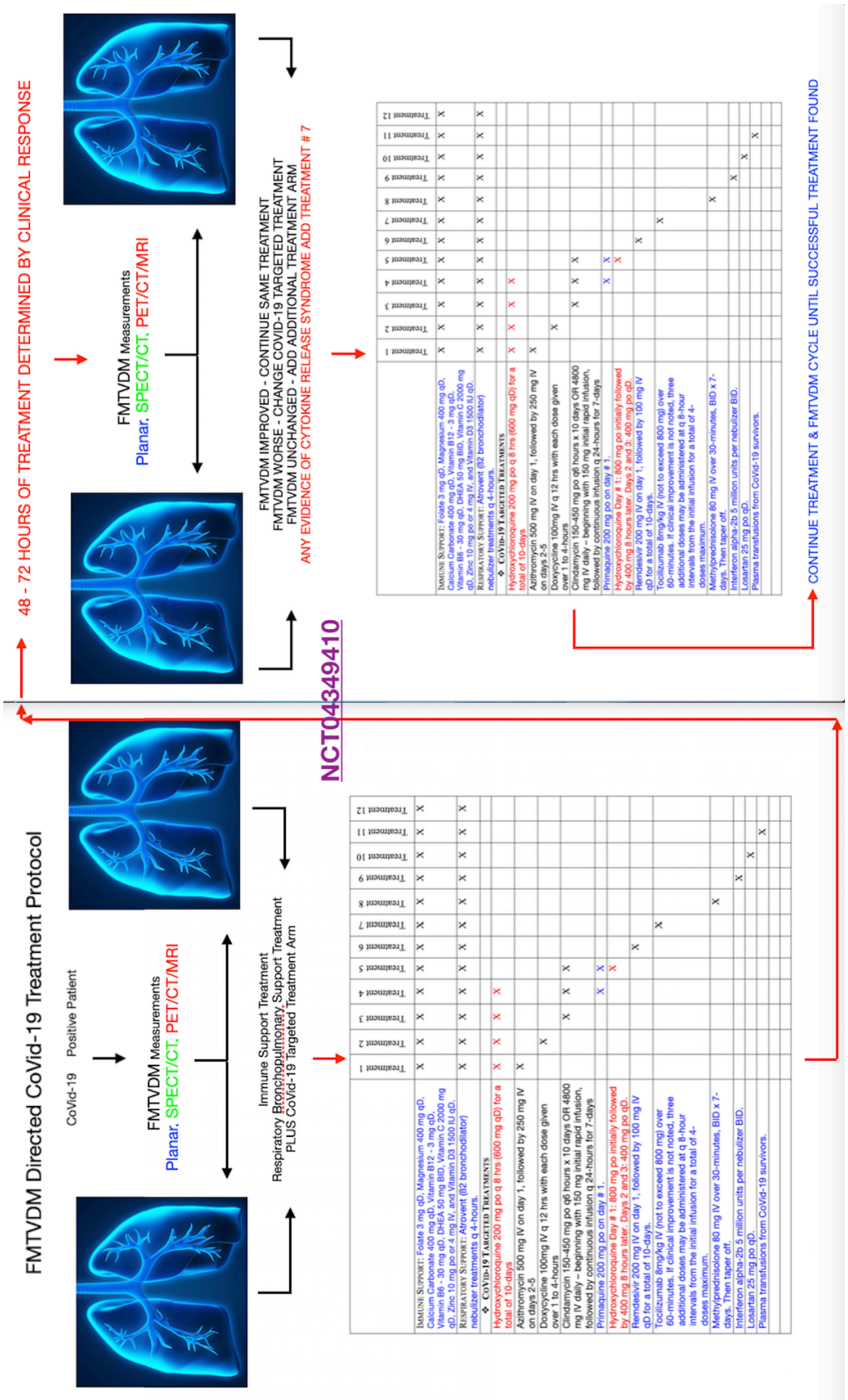
TABLE

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 *IS* quantitatively calibrated. Calibrated to that which the camera actually measures —scintillation emissions
Reported as	Normal, mild, moderate, severe, absent	Ratios: Derived from *time per injected radiation per patient body weight* **or** *Radiation per gram per volume*	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

Appendix E --- SCHEMATIC OF FINAL PROTOCOL SEQUENCE.



	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: Atrovent (ß2 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	

	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: Atrovent (ß2 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	

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

EXPLAINING WHY COVID-19 IS ASSOCIATED WITH INCREASED INFLAMMATORY DAMAGE AND THROMBOSIS.

https://rmfmd71.wixsite.com/fhhi-omnific/cytokine-release-sydrome-crs

The human body is designed to protect people from damage caused by something entering and harming the body. Three relatively common examples include:

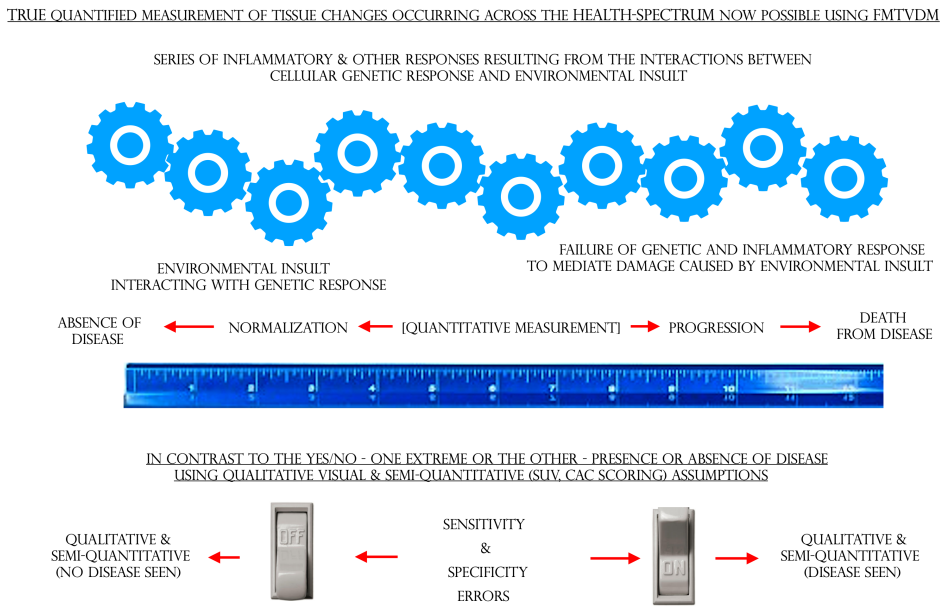
1) The introduction or ingestion of something into the body, which harms the body.

Damage occurring within your body caused by poor diets (too much saturated fat and too many calories - producing heart disease, and disease in other blood vessels causing strokes, claudication, impotence, etc.), chemicals (carcinogens - substances that cause cancer), pollution (air, water, land - e.g. fertilizers), smoking (chemicals you voluntarily put into your body), et cetera.

2) Cancer.

Changes occurring within your body, causing your cells to become abnormal and no longer function properly. These cells then threaten to take over the body.

It is the ability to measure changes in tissue metabolism and regional blood flow, using FMTVDM that allows us to measure both the extent and severity of Wuhan CoVid-19 infections before and after treatment to determine if a treatment is working or needs to be changed.

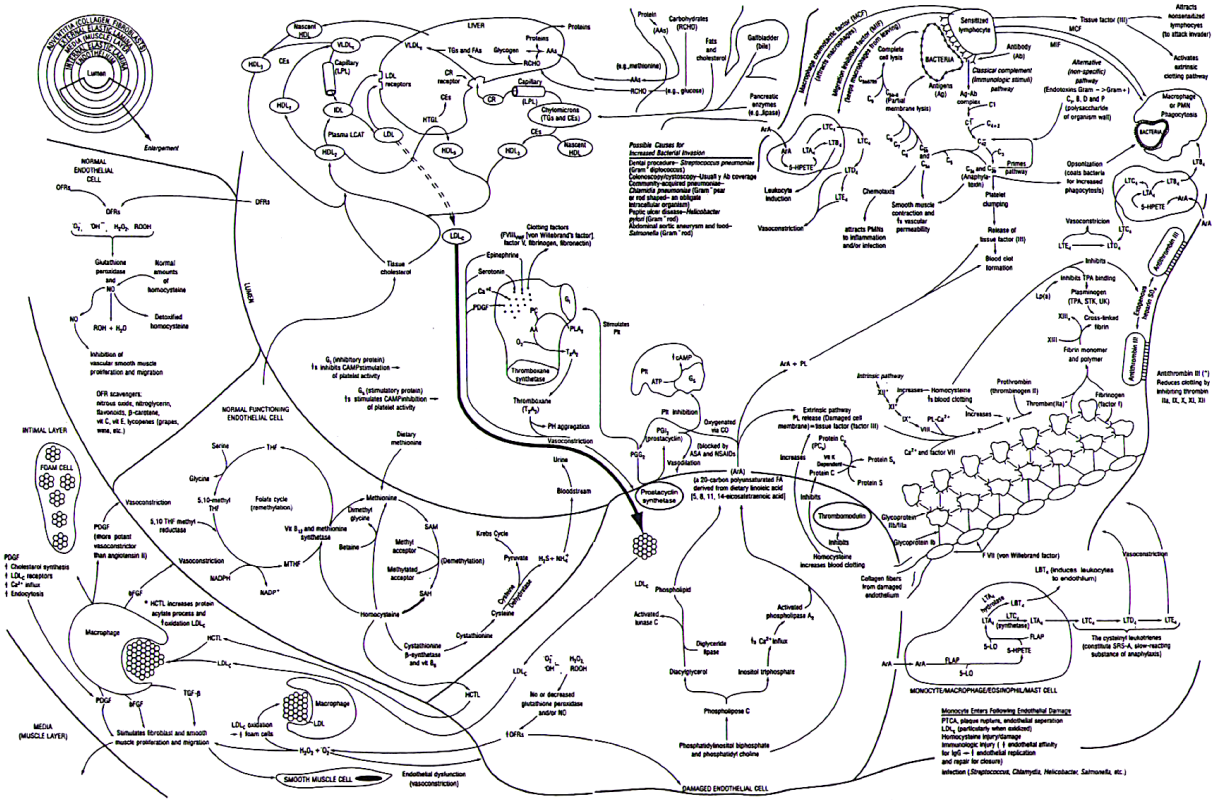


3) Infection.

This includes, among other things, fungal, protozoan, sexually transmitted diseases, bacteria, and viruses, like **CoVid-19**. These infectious organisms then try to live off your body so they can thrive and reproduce themselves at your expense.

To protect you, your body has the ability to fight against this damage using your immune system. These special cells talk to each other using chemical messengers called interleukins (e.g. IL-6) or cytokines.

The "Inflammation and Heart Disease[24]" Theory first discussed in 1995,then later published in the Cardiology Textbook [reference #3 on page 13] in 1999, was briefly discussed during a 20/20[25] segment in 2004, shows how the immune system is involved in this.



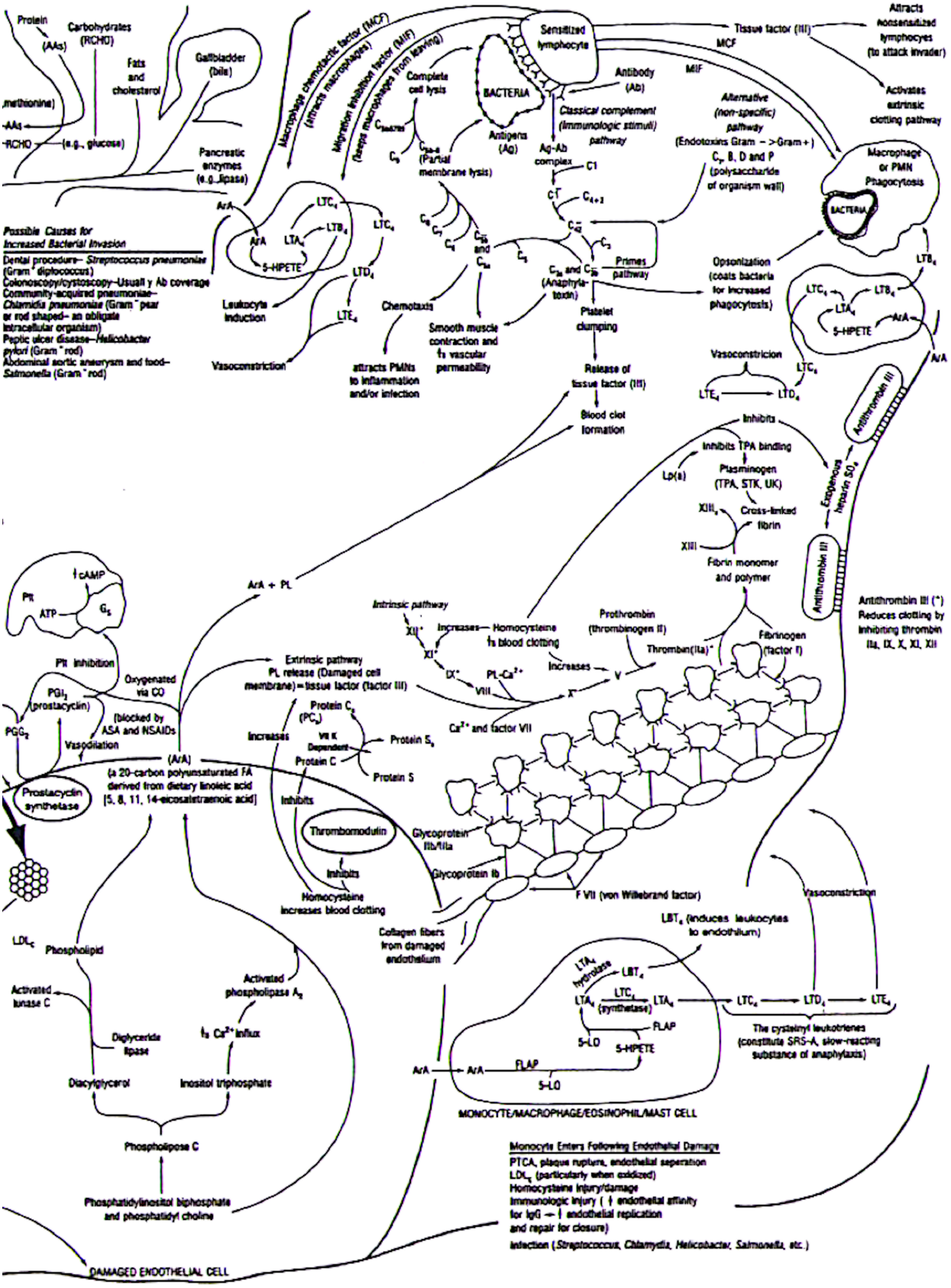
[24] Fleming-Harrington Redistribution Wash-in Washout (FHRWW) including stress-stress detection of inflammatory coronary artery disease. 1-655815511. Started 9-1-2011. Effective 9-16-2011, #TX 7-446-683.

[25] https://www.youtube.com/watch?v=Hvb_Ced7KyA&t=22s

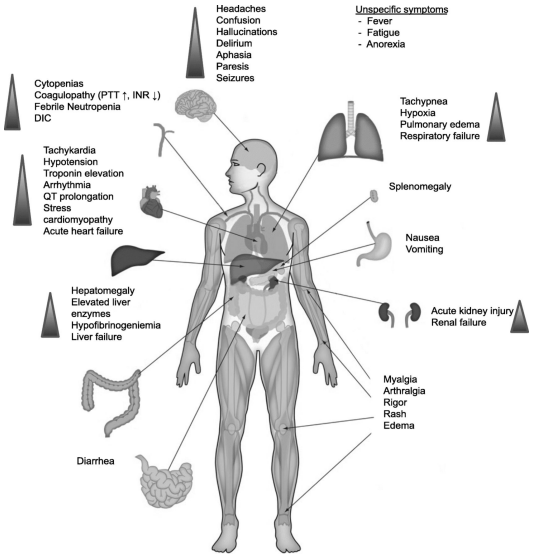
While there is a lot of information present in this one figure, if we look only at the right half of the figure (on the next page – p. 63) you can see how these infections, the chemical messengers used by your immune system and the compliment clotting cascade (chemicals in your body designed to recognize a problem and form blood clots), all work together to try to remove this harm and restore your body.

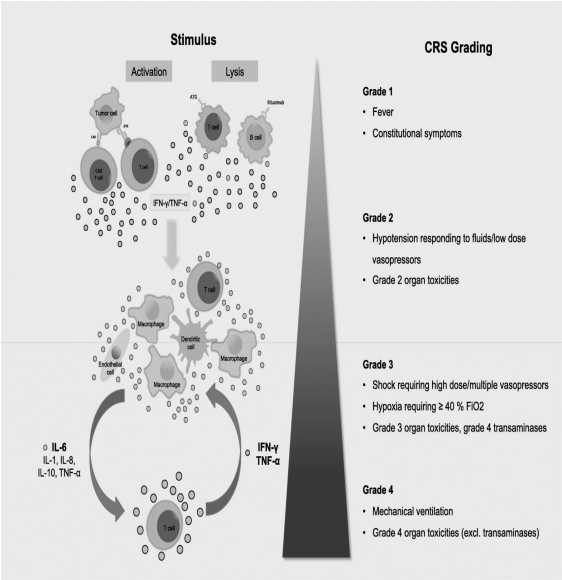
If the reaction to the damage - including that caused by the Wuhan CoVid-19 Virus - is too little, the body cannot heal itself. If however, the reaction is too much (for a variety of reasons including the presentation of a virus which your body has never seen before), then the very process designed to protect the body can actually cause harm to the body.

Much like dropping a nuclear weapon on a city. It will wipe out the enemy, but there will be nothing left in its wake and you won't be able to send troops in because the area is toxic and will only harm your troops.


Protein
(AAs)
Carbohydrates
(RCHO)
Fats
and
cholesterol
Gallbladder
(bile)
Pancreatic
enzymes
(e.g., lipase)
(e.g., glucose)
Possible Causes for
Increased Bacterial Invasion
Dental procedure– Streptococcus pneumoniae
(Gram + diplococcus)
Colonoscopy/cystoscopy–Usually Ab coverage
Community-acquired pneumoniae–
Chlamidia pneumoniae (Gram – pear
or rod shaped– an obligate
intracellular organism)
Peptic ulcer disease–Helicobacter
pylori (Gram – rod)
Abdominal aortic aneurysm and food–
Salmonella (Gram – rod)
Macrophage chemotactic factor (MCF)
(attracts macrophages)
Migration inhibition factor (MIF)
(keeps macrophages from leaving)
Sensitized
lymphocyte
Tissue factor (III)
MCF
MIF
Attracts
nonsensitized
lymphocytes
(to attack invader)
Activates
extrinsic
clotting pathway
Complete
cell lysis
BACTERIA
Antibody
(Ab)
Classical complement
(immunologic stimuli)
pathway
Antigens
(Ag)
Ag-Ab
complex
C1
Alternative
(non-specific)
pathway
(Endotoxins Gram – >Gram +)
(polysaccharide
of organism wall)
(Partial
membrane lysis)
Macrophage
or PMN
Phagocytosis
BACTERIA
AA
5-HPETE
Leukocyte
induction
Chemotaxis
Vasoconstriction
attracts PMNs
to inflammation
and/or infection
Smooth muscle
contraction and
vascular
permeability
Platelet
clumping
Release of
tissue factor (III)
Blood clot
formation
Primes
pathway
(Anaphyla-
toxin)
Opsonization
(coats bacteria
for increased
phagocytosis)
Vasoconstricion
Inhibits
Inhibits TPA binding
Plasminogen
(TPA, STK, UK)
Lp(a)
Cross-linked
fibrin
Fibrin monomer
and polymer
Exogenous
heparin
Antithrombin III
Antithrombin III (*)
Reduces clotting by
inhibiting thrombin
IIa, IX, X, XI, XII
cAMP
PIt
ATP
PIt inhibition
Oxygenated
via CO
(blocked by
ASA and NSAIDs
Vasodilation
Prostacyclin
synthetase
(A/A)
(a 20-carbon polyunsaturated FA
derived from dietary linoleic acid
[5, 8, 11, 14-eicosatetraenoic acid])
A/A + PL
Intrinsic pathway
Increases
Homocysteine
blood clotting
Prothrombin
(thrombinogen II)
Thrombin(IIa)
Fibrinogen
(factor I)
Extrinsic pathway
PL release (Damaged cell
membrane) = tissue factor (factor III)
Increases
Protein C
(PC)
Protein S
Protein C
Inhibits
Thrombomodulin
Glycoprotein
IIb/IIIa
Glycoprotein Ib
F VII (von Willebrand factor)
Homocysteine
increases blood clotting
Collagen fibers
from damaged
endothelium
Vasoconstriction
LBT (induces leukocytes
to endothelium)
LDL
Phospholipid
Activated
lunase C
Activated
phospholipase A
Diglyceride
lipase
Ca influx
Diacylglycerol
Inositol triphosphate
Phospholipase C
Phosphatidylinositol biphosphate
and phosphatidyl choline
DAMAGED ENDOTHELIAL CELL
FLAP
5-LO
5-HPETE
The cysteinyl leukotrienes
(constitute SRS-A, slow-reacting
substance of anaphylaxis)
MONOCYTE/MACROPHAGE/EOSINOPHIL/MAST CELL
Monocyte Enters Following Endothelial Damage
PTCA, plaque rupture, endothelial seperation
LDL (particularly when oxidized)
Homocysteine injury/damage
Immunologic injury (endothelial affinity
for IgG — endothelial replication
and repair for closure)
Infection (Streptococcus, Chlamydia, Helicobacter, Salmonella, etc.)

This excess is exactly what is talked about in the "Inflammation and Heart Disease" Theory and what accounts for the CoVid-19 problems (ARDS, strokes, blood clots, skin lesions, etc.)





Blindly treating CoVid-19 without measuring what is happening at the tissue level, is asking for trouble. Not addressing Cytokine Release Syndrome (CRS) or clotting[26] problems (pulmonary emboli, deep venous thrombosis, etc.) is asking for problems. Not treating patients with Acute Respiratory Distress Syndrome (ARDS) accordingly, has arguably lead to many ventilator deaths.

That is why NCT04349410 not only includes a treatment arm to address CRS, but requires FMTVDM measurement of what the treatments are actually doing to the CoVid-19.

As detailed in the “Inflammation and Heart Disease” Theory, viruses and the immunologic response to viruses, result in an inflammatory reaction that causes the release of cytokines and clotting. This reaction has both a local and systemic effect, which must be addressed to successfully treat the patient. There is the expectation that the presentation of a virus like CoVid-19, which has not previously been seen by the patient, may result in an intensified reaction as the immune system attempts to address the infecting organism.

Without FMTVDM measurement to objectively show clinicians what the treatment is doing to the virus, we are only guessing.

[26] All patients without contraindications should be placed on Heparin 5,000 units SQ BID if they are immobilized or confined to bed. Further treatment should be provided as clinically indicated.

appendix G. Fleming FMTVDM Treatment Protocol effective 4 July 2020

FMTVDM Directed CoViD Proposed Treatment Guideline NCT04349410

Pre-hospitalization	Hospitalization and Evaluation of CoViD Severity on Day 1.	Acute Innate Cytoxic Immune Response Treatment on Day 1.	Oxygenation Begin on Day 1.	Evaluate Treatment Response FMTVDM Day 3.	Delayed Adaptive Humoral Immune Treatment. Day 3 immediately after FMTVDM.
Pre-hospitalization	FMTVDM measurement of CoViD.	Initiate Additional Treatment	Use incentive spirometry for Rx and measure of respiratory strength.	FMTVDM measurement to determine Rx effect.	Adjust Rx given FMTVDM results.
For symptomatic individuals begin HCQ, AZT and/ or alternative inhibitors of viral transcription or protein translation.	Begin pre-hospitalization Rx if not already started.	Bronchodilatory Beta-2 agonsit Rx.	With any compromise in ventilatory status begin PRONE positioning of patient.	(1) Improved. Cont Rx. (2) Stable. Add next level of Rx. (3) Deterioration. Change Rx.	Initiate Remdesivir if not already started.
	ECG and Rx any prolongation of QTc with Esmolol, K, Ca, & Mg.	Consider adding Primaquine 200 mg one dose.	Consider BiPAP		Initiate methylprednisolone.
Begin Immune supportive Rx including Zn.	Measure inflammatory & thrombotic markers and treat accordingly to address and prevent clotting and further uncontrolled inflammation.	Initiate Tocilizumab.	Prepare for VV or VA ECMO support.		Continue to aggressively address inflammatory and clotting disorders including efforts to get patient out of bed (chair, ambulate, etc.) to avoid further thromobotic episodes.
Consider combination administration of interferon alpha 2 beta treatment with other agents.	Do NOT merely leave patient in bed (chair, ambulate, etc.).	Initiate interferon alpha 2 beta. Consider Remdesivir.	If other measures fail consider ventilatory support with VT not to exceed 5 cc/kg IDBW.		Consider passive immunity with plasma with attention directed to potential associated clotting potential.