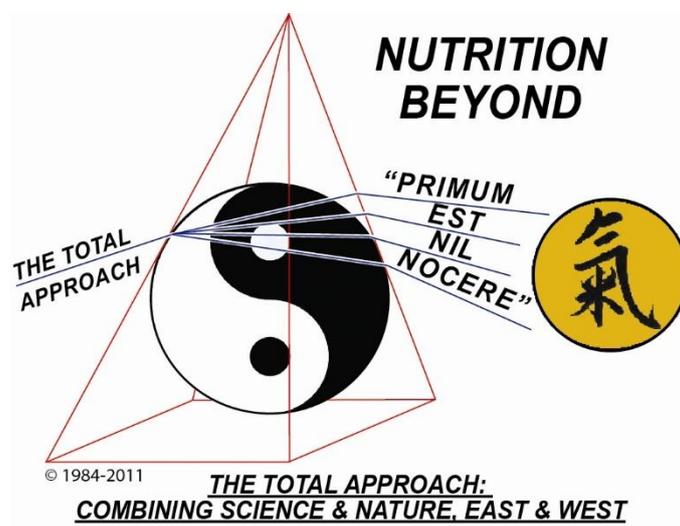


COVID-19: CONTAGION to Pathological/Lethal MORBIDITY to MORTALITY

THE Road to Perdition...and HOW to Avoid It: The LAST WORD



Pt.4:

My ResearchGate (the Scientists' Forum & Journal domain)

Posting # 2: In reply to Dr.Rosita Dangmann's request, PLEASE read the following article, towards the end as to the time-line I can address this in detail. Meantime, I would like to finish on what I started about the "*Cytokine Storm*" a few days ago...

WHEN to Intervene in the "Cytokine Storm?"

BEFORE we begin, some "light relief":

Quotable Quotes

These few "gems" by Gov.Andrew Cuomo:

"DON'T be reactive; you NEED to be pro-active"!

(A few days after my Pt.1 newsletter in which I said "*The Best form of Defence is...Offence*" a Shaolin kung fu tenet). **Cuomo said:** "*Don't be on the Defence (Defense – American spelling).....BE on the Offence*".

On March 31, he said: "*We've been behind it on Day 1 since it got here. And we've been playing "catch up". You DON'T win by playing "catch up". We have to get ahead of it*".

"The 2nd Rule is: NEVER underestimate your opponent....and we under-estimated the Virus...It has proven to be much more powerful & dangerous than we expected....And the 3rd. point is:

*PLAN forward, get AHEAD of it! Anticipate the next "BATTLE" **and** plan for it (exactly my Modus Operandi"!)*

"This Virus spreads like a fire thro' dry gras, with strong wind behind it..."

When New York city had its first 600-death day, he said: *"This spreading like a bullet train!"*

I would say it like this: *"This "Thing" is NO longer a "Freight Train" irreverently ploughing its way thro' populations any which way; it is NOW a "bullet train" smashing its way thro ANY population ANYWHERE"....*

This was from 1 of the Media people at a White House Press Briefing: *"We're at War without ANY ammo!"*

OK, this is my quick preliminary Reply to Rosita of this Forum who said: ***"Which factors could influence the outcome of COVID-19 patients and which alternative intervention possibilities could be applied?"***

We're headed there in probably a week's time or more....As I mentioned a few days ago, we started a BIG Newsletter Series (of 12 or more long, detailed postings) several weeks back. & NEXT, I will be drilling down to the 4 main forms of the Immune System, of which 3 are major [**Intrinsic** (eg. Inteferons, Autophagy, micro-RNA, etc.), **Innate**, & **Acquired/Adaptive**] & 1 somewhat "Experimental" form [**Convalescent Plasma Therapy (aka Passive Antibody Therapy)**, something un-proven against this virus]. And after that, we'll get down to some advanced Nutritional Medicine [ALL with their respective published Clinical Evidence]

For the antecedents to this, please read the start ('The PRELIMINARY') of our Series [COVID-19: The EQUALIZER Series] & the 3 that followed that (I have uploaded them here in our new RG membership). We're building this up in a logical sequence; The next to come out (hopefully in the next day or two) will be this close look at our Immune systems.

One more word about my expose` the other day on the "Cytokine Storm". I gave you all a glimpse of the Inflammatory dynamics at work. The thing I forgot to mention is that these Inflammatory cytokines are not ALL "bad" – in 'Inflammation Dynamics, there is NO such thing as such thing as 'something being TOTALLY & ALL bad. It starts out "good" to serve a purpose, but when that "purpose" is not attained (for whatever reason) is not attained (for whatever reason, and there are lots of that!), then its continued influence is bad (it CAN be real bad!). In infections [as in most, if not all, other Acute-Phase situations], the Inflammatory enzymes & Chemokines are pumped out in an attempt to deal with the microbial invader(s) - they marshal all the leucocyte members (of the various Immune Systems) to "do battle". IN a realistic time-frame, IF successful, this phase should last from 1 - 3 weeks. IF by the end of 2 weeks, the temporary upward-exponential curve doesn't flatten and the symptomatology keeps

getting worse, you KNOW the "Fight" is NOT going to be successful. By the end of the 3rd. week, IF the sero-IgM is still high (OR, worse, still rising) you should know the "Fight" is almostLOST.

WHAT would then be happening with the so-called "Cytokine Storm"?

Well, via the body's -ve 'Feedback' loops [eg. DCs, B-cells, TOLL-like receptors (TLRs), etc. One example: the surface-borne TLR10 can "sense" the exosomal presence of a flu-type virus at the point of its "docking" operation (for COVID-19, it is ACE2 – see our Pt.1 article) with the host cell. There are many other sensing cytokines that can "tell" the body that the Virus is STILL there, undefeated [THAT is WHY it ramps up the "Storm"...]. BUT it doesn't know whatelse to do except keep driving the "Storm"....In fact, if anything, it WILL ramp up the "Storm", in a vain & futile attempt to drive more neutrophils & other Leucocytes into battle [NK, DCs, monocytes (to generate more macrophages & other phagocytes), T-cells, Defensins, etc, etc.] to the "sites of battle". Clinically, IF the Neutrophil count:Total Lymphocyte sero-count **ratio** is > 10, the **Px is going to be in a REAL rough, tough time....** (IF the ratio is around 6, the Px prognosis will bebetter)

The increasing tide of Inflammatory cytokines WILL inflict MORE damage for sure on those body parts I previously mentioned. Not to mention the direct damage inflicted by this type of Virus....DON'T forget: THIS Corona-Virus is much larger, **physically**, than ALL previous corona-viruses (*it IS the BIGGEST "bully-boy" of ALL the Corona-viruses we've ever known before....*). The damage inflicted by it is **vicious, resolute, pathologically morbid.....** it's like millions/billions of very tiny razor-blades cutting up your insides - **THIS is downright scary!** People in Lombardy (northern Italy) & Spain had reported severe pains in their lungs, hearts, kidneys and small & large intestines....Many had coughed up blood AND seen blood in their stools; several others just fell into a coma & never woke up....

The thing I wanted to emphasize here was the timing of the anti-Inflammatory intervention. Understanding as we do that pro-Inflammatory cytokines are modulators – they're NOT "bad" all the time (THAT'S why they're modulators). You do NOT institute an anti-Inflammatory strategy at the beginning of experiencing the symptoms or (in the case of the asymptomatic people) when a proper test (a RT-PCR one) shows up +ve and then impose a "selective blockade" on the COX2 members (*see my last & very 1st posting here, on RG, just a few days ago*) or even the "Pope" right at the top of the Inflammation "tree", **NF-KappaB**; even NF-KB himself HAS a modulatory role to play at this early stage.... You give the "Storm" a short-term leeway to do its thing, ie. you DON'T "interfere" with it right from the word "go!". SO, HOW long have you got to play with?? Remember, this IS a "novel" Corona-Virus & NOT too much is known or predictable of its "time-line".... We can only learn from Wuhan, Lombardy Province, Milan, Madrid, and now New York, the places where the Virus has "played its strong hand".....

IF by the end of the 2nd. week, & Px looks bad, you know his “fight” with the Virus most likely CANNOT win, and you NOW have to seriously consider “culling” the “Storm”, if not shutting it down completely (which would be TOTALLY impossible, NOT if the Virus is still around in the body). It IS the case of the lesser of the 2 “evils”: ***the Px either dying OR still alive, but in terrible pain....*** At that point, you have NO choice but to move in AND limit the contributory damage from the terribly high levels of the “Storm”. You DON’T have much “room to move” here.... At this point, you MUST try to limit further combined damage (from BOTH the Virus AND the Inflammatory cascades) to the Px’s upper airways, lower airways (including the lungs), the heart, kidneys, & intestines... You have to move in NOW & start, IMMEDIATELY, the TOTAL anti-Inflammatory strategy – ***inhibit*** ALL the drivers of COX2 and 5- & 12-LOX (especially the latter generating the Leucotrienes which are like “permanent residents” in ALL the airways!). From this highly “critical point” onwards (his hs-CRP would be “mile-high” at THIS point!) and the ***Inflammation alone can “finish” him off....***(remember what I said of the “Lesser” of the 2 “evils”?? It COULD turn out to be the “game-changer” in the Final analysis....)

What about the “quintessential good-guys” (as how I described them before): the ***COX1 Pathway***, leading us to THE most powerful anti-Inflammatory enzyme, PGE1, in the human body ? ***WHEN do we ramp him up??:***

At the beginning (as defined above) OR 2 – 2 ½ weeks later (when it looks obvious the Px won’t win the fight against the Virus).

Prostaglandin E1 works ***independently*** of ALL the COX2 products (even PGE2) & ALL the Leucotriene products [even LTB4 – the MOST damaging enzyme to the airways (upper & lower) & the lungs....]

SO, you deploy the COX1 drivers ***right at the beginning....*** Matter of fact, if you’re smart & want to be “pro-active” right at the beginning (whether you have a COVID +ve test or not), you would start driving up the COX1 straight away....

Our next Newsletter (mapping out the extremely intricate human Immune systems) posting might actually take 2 parts, considering the subject is so terribly complex....When I’m thro’ with that, THEN we can get down to the “business end” of dealing with the subject of ***“Defence AND Offence”***... Remember, they’re one (read my Pt.1).

One last word here: I just DON’T get it that “they” (Doctors in America) DON’T get it OR “haven’t gotten it” by now! One of the articles in the latest edition (April 6, 2020 – 5 days ago) of ***“Scientific American”***:

Heart Damage in COVID-19 Patients Puzzles Doctors

Up to one in five hospitalized patients have signs of heart injury. Cardiologists are trying to learn whether the virus attacks the organ

Here, read this article: [This "PUZZLE"](#)

WHAT is it that they (these Doctors) DON'T get?? THIS is HOW America got "caught with its pants down" – "playing catch-up", a lingo used by Gov.Cuomo. **Guys, DO your "home work", read the Research....**

Dr.L.S. Macloud, Ph.D. (Cambridge Univ.)