

Commentary

The new nucleic acid based COVID-19 vaccines: a glittering achievement, yet disturbed by a black stain that does need to be identified and swept away

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Some two years ago, a that far untold plague fell onto our heads without notice. Presenting initially with a harsh pneumonia destroying lung alveoli, SARS COVID 2 (SCVID2) reached rapidly the feat to kill over 80% of the older sick people in retirement shelters, and met the requirements to be classified “pandemia” since March 11, 2020. To honor the trust placed on it right at the beginning, SCVID2 promptly trespassed the age limits of candidates to the infection. Sweeping away thousands of youngsters and middle-aged, the virus soon made outdated the label of an “older-bound” pathogen, and, to make the old story short, today’s dash board is giving: 645.630.482 infected, and 6.634.816 fatalities. The overall mortality might be 12-2%. It seems that no disease presentation, whether human or animal has been missed by this protean virus. Has the COVID 19 syndrome disappeared, or (at least) is it walking its sunset strip? This issue is being increasingly debated by media in the last weeks. The very fact that is being “debated” might be appalling per se. The simple possibility that the infection adopts an endemic course (meaning: silent low level viremia affecting the people only episodically), is reported to erratically switch on panic in those who never-the-less tolerate close contact with unrelated pathogens : thus, our brain seems to be incurable in conceiving SCVID2 as the “pre-historic evil”. The ability of SCVID2 to mimic the true COVID syndrome even when given as a vaccine, is now making things even harder, fostering the irrational disappointment of those raised since their infancy with the dogma that vaccines “can only be good”. In the attached Editorial, we chose to concentrate on these cases, trying to help knock down rising superstition, now the best allied of COVID 19. On the turn of the second year, pandemics are known to try and escape counter-measures, by hiding beneath a

cloud of forgetfulness. Allowing this outcome to terminate our COVID combat now, means deadly defeat. Teaming up to devise and launch the final hit must hold in our scope to the very end.

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Background

After two years, the data now in our hands show that we have been hit (and still we are) by an yet untold killer virus, as reinforced by a rough dashboard: total infected <643. 875.406; fatal outcome <6.6.08230. 12.998.974.878 vaccine maneuvers; 1.1%, toxicity. The relevant pandemic that subsequently broke out was officially named SARS-CoV2 pandemic (after the virus). The identification COVID-19, rapidly reaching top people's favor, does in fact represent a misnomer. The European Medical Authority Board had intended this label for the clinical pictures that may follow the initial SARS infection. No matter what bureaucracy really wanted, this new threat to Mankind survival early in 2020 had already marked a milestone^[1], for the few reasons examined below.

Main Text

1) Apart from the “historic Spanish Flu”, in 1918, associated to a world death toll of some 50 million, (the argument for the many school studies of all-time), very few or no one of our contemporary neighbors can readily provide an adequate reply if interviewed on any in-depth question on this yet appalling event. Simply, the Covid 19 just “came out of the blue” for most mortals on earth. 2) The allegedly infectious cause (SARS-CoV2) is piling up on itself a few tempting curiosity reason, including 3) a mysterious pre-historic origin^[2], which, nevertheless, has not been convincingly disentangled from possible trivial loss of contact between the virus and its watching policeman in a Chinese market shuffle; The Corona(s) seem to be endowed with an utterly potent pro-inflammatory, and pro-coagulative apparatus^[3] capable to rapidly place patients in jeopardy, and lead supervising Authorities to strongly advise upgrading and placing Coronas to higher levels of defense guard. This circumstance, coupled with a ounce of genuine curiosity, has finally deserved a level of clinical attention, when the degenerative CNS diseases (Alzheimer's, Parkinson's, Creutzfeldt's) were shown recently to have engaged the fastest gear again, preparing to climb harder incidence peaks. We purportedly confined our efforts to achieve a closer

scrutiny of the relationship COVID 19- infected hosts. The well-known hyper-inflammatory potential of the COVID agents proved in many cases to be an irresistible temptation to dissect the pro-inflammatory virus role, as opposed to the cell defensive arsenal. An excess of active fibrinogen, in tandem work with a propensity to easy intravascular coagulation, may end up with the devastating formation of intravascular masses of transformed atypical fibrinogen, leading unavoidably to diffuse ischemic damage.^[4] At this point, one can readily understand that a punctual classification of the heterogeneous materials floating within patient's vessels will be crucial to understanding immediate reactions and immediately following strategies. Large systematic studies mostly based on the master experience of the German Professor Paul Ehrlich in varied times of the 19th century taught us -and thousand of highly committed pathologists- the way to perceive the dramatic difference between microscopic deposition of fibrin powder in "common" atherosclerotic subjects, as opposed to the nascent hyaline networks (harbingers of the giant thrombi dealt with here) that might "(typically)" be appreciated in the lumen of cerebral vessels, as belonging to subjects undergoing a diagnostic autopsy ^[5] following COVID-19 infection, either spontaneous, or (fortunately a minority) in temporal coincidence with a vaccination session. Vascular surgeons have often treasured such autopsy findings because providing clues to the effective choice amongst as many tentative treatments as: injection of dissolving solutions, alone or in combination with the positioning of intra-vessel filters preventing floating debris to reach and block blood supply to the heart; careful surgical debridement of the mostly diseased vessel connections. These premises really do involve matters (at an equivalent relevancy level) of legal medicine and emergency vascular correction, with an obvious interdependence. Building up a severity rank will help establish the appropriate level of therapy as a function of the intervention risk; The other crucial point stems from the high level now reached with our etiologic scanners i.e. the detection of involvement of proteins into the pathologic coagulation chains. Thus, we believe that a simply operational take-home message can pivot on the above notes: 1) A classification must be modeled onto a cause-effect interpretation key; 2) Search for the existence of prion-like entities^[6] and, if found, definition of the causative role. In lines of theory, COVID-deriving proteins (the SPIKE holding the utmost importance), can exert the centrally conceived denaturing (coagulative effect) on host proteins through three main interconnected pathways.

A. The exuberant pro-coagulative power carried-in by the COVID-expressed protein (the already cited SPIKE, but others also) may well exert the two synergic roles of protein dys-figurement (specific of prions) and induction of tissue hypoxia. These details are mastered in the smart companion paper^[7] authored by Chakraborty *et al.*

- B. Other teams, stressing the same points, have imagined an additional source of damage, favored by the delicate intranuclear positioning of the nascent SPIKE protein domains: random bumps of SPIKE debris with sub-cellular host membranes, could ignite newly elusive inflammation facilitators.^[8]
- C. We ourselves,^[9] reiterating a closer scrutiny of the entire material, were struck by the poorly emphasized possibility that a fully working coagulative prion may become disguised as a Spike Protein. This construction would imply autonomous roles of COVID proteins, rendering redundant any emphasis on supervening other pathogens in the coagulation cascade, despite attention on this pathway being stressed by authoritative names.^[10]

SPECIFIC DECISION MAKING in the light of the above elucidation

No matter how fussy our criticism can be against the nucleic-acid-based recently launched vaccines, obviously conceived to cripple COVID-pandemia, one must agree that planning a new agent from base 0 would be inadequate at this time of the initial viral attack. Instead, we deem it reasonable to try and theoretically discuss a couple of options.

In our opinion, it would be desirable to progressively loosen the “obsessive” fuss focused until now on the search of a T-cell based vaccine, tentatively exploring instead, the offer from the innate, non specific pathways, with a specific eye to: -- Relative ease of preparation; -- Species specificity, against no viral specificity; immediately effective upon injection. We have reported some extra details of a project involving (as stimulator “fake” virus) the handy use of synthetic polynucleotides (Poly:IC *et al.*), making reference to a few ongoing NIH trials.^[11]

Indeed, it is easy to anticipate that those men/women, battered for months in the absence of any shelter, could have accepted any thing presented as an anti-viral weapon. We deem that administration of the SARS virus as a cutaneous patch that can be squeezed under one’s fingertips, does raise a kind of reassuring “glow” that can not be released from the pharmacy cartoons fallen from a military jet making its silent path 36 thousand feet amongst fluffy clouds over the operation camp.^[12] Relevant data did also reaffirm that acceptance or perplexity do depend on the class of information which people get exposed to, the pre-information mind state, and the ease to trust authorities. All-in-all, at the moment we are feeling most keen at placing our trust on trained-immunity vaccines,^[13] as antigen non-specific agents but ready to go, as functional stimulators of Interferon, which in turn can exploit the antiviral efficacy of the NK cells to a large extent. To perhaps trying to terminate this sort of “passionate plea”, we find it adequate to remind that real life trials have readily demonstrated the best adherence levels from workers

deployed in any activity and involved with decision at any stage, than those kept apart from active participation^[14]. Finally, we were hit by seeing a delicate psychologic issue^[15] almost resolved in a pretty military initiative.

Such programs, which are largely based on a critical role of IFN, will require a pedantic search for the relatively common non-function IFN variant; such variants are known to hamper timely switch from IFN to T-cell mediated responses, a step which, if failing, is known to dramatically detract from the success of any anti-viral immune response.^[16]

Needless to say, any pathway, whether present or future, directed to defining all reasonable anti-COVID strategy will have to be strictly revised, reappraised, and reinforced, taking as reference the impending multi viral attacks as per forecast by the main monitoring organisations.

Conclusively driving home: This neglected, sudden, harsh multi-viral attack last time came close to place his boots over our neck, and now no more is left before the combat bell tolls again within our still shivering ears. Confident teaming up and individual bravery, before it gets too long, should succeed in preparing the antidote to the next unknown attacker. The future, however, is not ours to see.

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