Potent NRF2-activating dietary supplements (like resveratrol, curcumin, sulforaphane, "Asea redox supplement" [ARS]) should be clinically tested as adjuvants in all types of medium and severe cases of aggressive respiratory viral infections (including Influenza A/B/C, SARS, MERS, COVID-19, measles, avian influenza etc.) based on their extrapolated cytoprotective antioxidant effects (especially on vital organs), including the cytoprotection offered by ARS on the cardiac muscle of DMD patients which can be extrapolated to the lungs (very short medical communication)

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For motivation of this Wikipedia-based paper format see URL

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Abstract
(with some abbreviations further used in this paper)

This very short medical communication proposes that potent NRF2-activating dietary supplements (like resveratrol, sulforaphane, curcumin, "Asea redox supplement" [**ARS**] etc.) should be clinically tested as safe adjuvants (in various combinations) in all types of medium and severe cases of aggressive respiratory viral infections (including Influenza A/B/C, SARS, MERS, COVID-19, measles, avian influenza etc., including those patients which have important comorbidities like HIV/AIDS, tuberculosis [**TB**] etc.) based on their extrapolated cytoprotective antioxidant effects (especially on the main vital organs: brain, heart, lungs, kidneys and liver), including the extrapolated strong cytoprotection offered by ARS on the cardiac muscle of DMD patients (which can be extrapolated to the lungs), like the author of this paper has demonstrated in past papers [**1**,**2**, **3**, **4**, **5**].

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I. Very short medical communication with main arguments and additional ideas

Introduction. Potent NRF2-activating dietary supplements (**NADS**) (like resveratrol, sulforaphane, curcumin, "Asea redox supplement" [**ARS**] etc.) stimulate the activity of NRF2, a master transcription factor (encoded by the NFE2L2 human gene), which activated NRF2 significantly increases the expression of antioxidant proteins (glutathione synthetase, glutathione peroxidase [**GPx**], superoxide dismutase [**SOD**], catalase etc.) that strongly protect against oxidative stress (**OS**)/damage triggered by acute/chronic infectious (viral, bacterial etc) or non-infectious (toxic, autoimmune etc.) injury and inflammation at cellular and tissular level. Several NADS are being studied as treatment of diseases that are caused by OS (or which have an important OS component in their pathogenic chain) [URL1, URL2, URL3, URL4].

For a more detailed introduction to NRF2 and ARS see the main references of this paper [1, 2].

The author has also dedicated a separate online database [URL2] to all known (natural or synthetic) NRF2 activators (see URL): www.nrf2.dragoii.com

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The main proposal/suggestion of this short medical communication. *In the context of recent various aggressive viral epidemics worldwide (including Influenza A/B/C, SARS, MERS, COVID-19, measles, avian influenza etc., including those patients which have important comorbidities like HIV/AIDS, tuberculosis [**TB**] etc.), this paper proposes that at least some of the previously listed NADS (including ARS) to be clinically tested in high doses (or even very high doses, close to their toxic lower bounds) as adjuvants (in combination with specific antiviral drugs or other types of medication) in all types of medium and severe children and adult cases of aggressive respiratory viral infections (as those previously enumerated), especially in those patients without prior vaccination against one or another specific disease (if, when and where it is the case).*

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Prediction (with arguments plus extrapolation). "ASEA redox supplement" (**ARS**) may plausibly show much stronger cytoprotective antioxidant effects than other NADS on vital organs (possibly affected by the aggressive viral infections previously listed) at average, high or very high ARS doses of 3-5-7ml/kgbm/day (**kgbm**=kilogram of body mass). **Argument (1)**. ARS has remarkable antioxidant and immunomodulatory effects (by NRF2 selective activation and NF-kB inhibition). *In vitro* studies showed that ARS is a very potent selective NRF2 activator, thus a very potent (indirect) cytoprotective antioxidant: the studies conducted *in vivo* also support this main pharmacological mechanism of ARS, with no toxicity up to high doses. **Argument (2)**. In both cases of children with Duchenne muscular dystrophy (**DMD**) (treated with ARS) published until present [1, 2] (plus one additional third DMD child case, which is still under preparation to be also published in the near future), the author has demonstrated that the strong cytoprotective effect of ARS (*on both cardiac and skeletal type of muscles*) can be replicated in vivo, with excelent safety profile and NO measured adverse effects on the bone marrow and/or liver (by standard blood count and serum levels/concentrations of liver enzymes): more specifically, even after only three months of starting ARS treatment, the main skeletal and cardiac rhabdomyolysis markers (with very high initial serum levels, especially CK, CK-MB, and myoglobin) dropped significantly (down to 2-3 times lower than initial serum levels), with NO found toxicity until present.

Extrapolation. Given its high capacity of limiting myocardial damage (proved by significantly decreasing CK-MB in two DMD cases (also based on the high cytoplasmatic target-NRF2 concentrations in these main vital organs: heart, lungs, kidneys and liver) AND its higher bioavailability in the central circulation

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system (which also serves those vital organs), this paper predicts (by extrapolation) that *ARS may have strong cytoprotective antioxidant effects in the lung tissue too: furthermore, ARS has a strong additional advantage over the other NADS, because ARS can be administrated both orally and nebulized (as it remains stable in this nebulized form), thus ARS may reach even higher concentrations in the affected lungs of patients with moderate or severe respiratory infections (like those already listed in this paper)* (see also next additional arguments).

Additional argument (1) (for the previous extrapolation). A trial in patients with chronic obstructive pulmonary disease (**COPD**) using sulforaphane (a potent NADS, yet weaker than ARS) *improved* the initially reduced phagocytosis of bacteria (by alveolar macrophages from those patients with COPD) [URL1, URL2].

Additional argument (2) (for the previous extrapolation). NADS may also have the additional benefit of improving resistance to viral entry and replication in cells infected with influenza A virus, thus may plausibly help in reducing COPD patient vulnerability to viral exacerbation [URL1, URL2].

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Additional ideas of clinical testing/research of ARS in combination with N-acetylcysteine (NAC). (**1**) ARS stimulates the cellular synthesis of reduced glutathione (**GSH**) (by activation of glutathione synthetase via NRF2 pathway), which is a very potent endogenous antioxidant. On the other hand, N-acetylcysteine (**NAC**) serves as a prodrug to L-cysteine (which is a precursor of the same GSH): hence, oral and/or nebulized (and/or intravenous) administration of NAC replenishes GSH stores of human organism and that is why it may strongly enhance the beneficial effects of ARS (by plausible therapeutical synergy) in these type of aggressive infections but ALSO in many other type of diseases with an important oxidative stress (**OS**) component (infections, DMD etc.) [URL]. Vitamine B6 is also a candidate that may be used in combination with ARS (plus/minus NAC, plus/minus any other NADS) [URL]. Various combinations of two or more NADS may also be clinically tested. There are also several respiratory OS markers that can be used to asses the biological efficiency of ARS and NAC (in standalone or combined adjuvant therapies) [URL1, URL2, URL3]

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Conclusion. Given their strong antioxidant effects (by NRF2 potent activation), at least some NADS (including ARS) deserve future cohort studies on acute/chronic diseases that imply high levels of tissular oxidative stress, especially some acute/chronic cardiovascular and respiratory diseases like: medium and severe infections (including aggressive infections like including influenza A/B/C, SARS, MERS, COVID-19, measles, avian influenza etc., including those patients which have important comorbidities like HIV/AIDS, tuberculosis [**TB**] etc.), acute myocardial infarction with acute/chronic heart failure, stroke, chronic obstructive pulmonary disease (**COPD**), asthma etc. of both children and adults, so that NADS may help millions and even billions worldwide.

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II. References
(partially integrated as Wikipedia URLs in the main text of this paper)

[**1**] Andrei-Lucian Drăgoi (July 2019). (ASEA in DMD - CJBRT article - 20.07.2019) **The Remarkable Effects of "ASEA redox Supplement" In A Child with Duchenne Muscular Dystrophy – A Case Report,** Canadian Journal of Biomedical Research and Technology (CJBRT) 2019; volume 1, issue 4:8. ISSN: **2582-3663.** URLs: URL1a, URL1b, URL1c (CJBRT original sources); URL2a (Research Gate source); URL2b & URL2c (Academia sources); URL2d (Vixra source); URL3 (Research Gate **preprint** source). **See also the newly released related add-on paper (RG preprint)** *The 1st case report on the remarkable effects of "ASEA Redox Supplement" (ARS) in a boy with Duchenne muscular dystrophy (DMD) – periodic updates released after 20.07.2019 (the date of the official case publication in a peer-reviewed journal)* (DOI 10.13140/RG.2.2.23141.76002, URL to RG preprint).

[**2**] Andrei-Lucian Drăgoi (May 2018). (ASEA in DMD preprint – version 1.1 – 1.08.2018 – 13 pages) **The clinical and biological effects of ASEA ionized water /"redox supplement" (co-administered with L-carnitine and omega-3 fatty acids plus multivitamins dietary supplements) in a ~3-year-old boy with Duchenne muscular dystrophy (DMD) from Romania – a case report**. Research Gate preprint. DOI: 10.13140/RG.2.2.21420.36486. URL (Research Gate source). 2 Recommendations from: Syed Ismyl Mahmood Rizvi and P.F. Zabrodskii. The article based on this preprint was published in July 20th, 2019 under the title "The Remarkable Effects of "ASEA redox Supplement" In A Child with Duchenne Muscular Dystrophy – A Case Report" in the Canadian Journal of Biomedical Research and Technology (CJBRT) 2019; volume 1, issue 4:8. URLs: URL1a, URL1b, URL1c (CJBRT original sources); URL2 (Research Gate source)

[**3**] Andrei-Lucian Drăgoi (November 2nd, 2019). (Asea in DMD – conferința Râmnicu Sărat - 45 slides - 2.11.2019) **Efectele remarcabile ale suplimentului redox "Asea"® în 2 cazuri de distrofie musculară Duchenne la copil și potențialul terapeutic al Asea în bolile acute și cronice cu o importantă componentă de stres oxidativ celular.** Presentation and conference paper also published on Research Gate with DOI (of RG presentation): **10.13140/RG.2.2.28023.78240 [URL2]. URL1a** (Research Gate main source; see also URL1aa), **URL1b** (Academia secondary source). **URL1c** (Vixra secondary source), **URL1d** (GSJ secondary source), **URL1e** (dragoii.com latest variant source).

[**4**] Andrei-Lucian Drăgoi (August 30th, 2019). (ASEA in DMD 2nd case preprint - v.1.0 - 30.08.2019 - 10 pages) **A Second Case Report Regarding the Effects of "ASEA redox Supplement" in a ~5-year old boy with Duchenne Muscular Dystrophy from Bucharest, Romania (preprint)**. Research Gate preprint with DOI: 10.13140/RG.2.2.18399.41128. **URL1a** (Research Gate main source), **URL1b** (Academia secondary source), **URL1c** (Vixra secondary source), **URL1d** (dragoii.com latest variant source), **URL1e** (GSJ secondary source).

[**5**] Andrei-Lucian Drăgoi (November 23rd, 2019). (Ataluren in DMD - version 1.0 - 23.11.2019 - 5 A4 pages) **A proposed extension of Ataluren indications (with future deserved studies) in patients with Duchenne muscular dystrophy (DMD) caused by frameshift mutations of dystrophin gene associated with abnormal premature termination codons (PTCs) at distance from the site of that given frameshift mutation**. Research Gate preprint with DOI: **10.13140/RG.2.2.21648.76804. URL1a** (Research Gate main source), **URL1b** (Academia secondary source). **URL1c** (Vixra secondary source), **URL1d** (GSJ secondary source), **URL1e** (**dragoii.com latest variant source**).