

A Metabolic Perspective

Therapeutic Option to Manipulate Redox Control of Viral Infection

Dr. ROBERT MELAMEDE Ph.D., Cannasapiens 11/11/20

The main theme of this presentation is that metabolism controls life and all of its manifestations, including viral infections.

By understanding the physics of life, one can get profound insights into the origins and evolution of life.

Most importantly, by understanding the living process, we can guide how the flowing energy that is responsible for our existence, in a way that promotes health through knowledge, rather than illness through ignorance.

For Health, all body systems must balance pro-inflammatory biochemistry with anti-inflammatory activity!

The Immune, Nervous , and the Cardiovascular Systems are:

- Attacked by Covid
- Homeostatically balanced in response to free radical activity (production vs quenching)
- The origin of symptoms emerges from unbalanced pro-oxidant and anti-oxidant metabolic activity

Living systems are:

- far from equilibrium flow dependent structures
- They exist by balancing opposing flows to create: newness or to repair aging.
- Cells get older by moving closer to equilibrium.
- Excess carbohydrate metabolism promotes excess free radical production, the cause of aging.
- The dynamic metabolic balancing acts of life are all pervasive.
- Here we see the example of how the renin angiotensin system is an embodiment of these concepts.
- The Angiotensin Converting Enzyme (ACE2) is the receptor for Corona viruses and is active through the human body infecting many cell types.



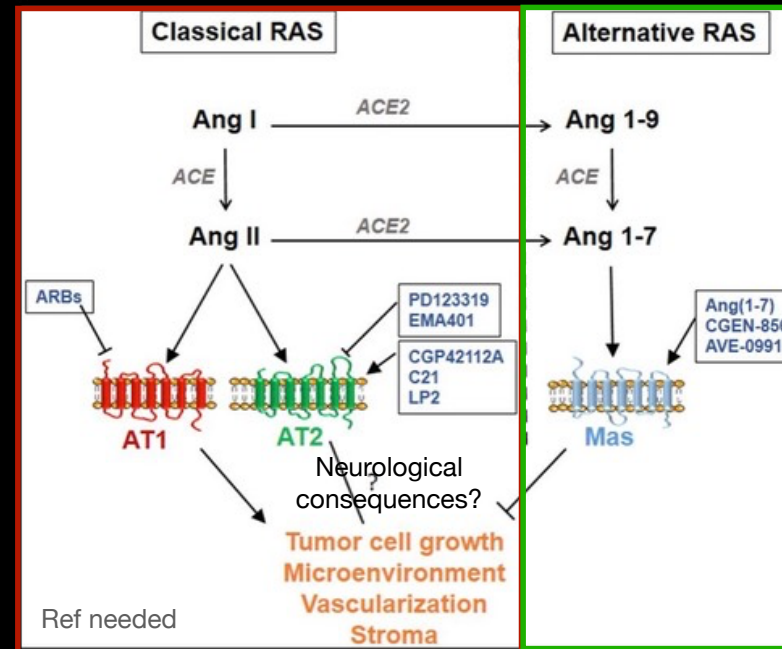
Corona Virus Infection

drbob

Inflammatory free radical
producing biochemistry
Powered by sugar/ami o acids

Anti-Inflammatory
biochemistry autophagy
Powered lipids

THE RENIN-ANGIOTENSIN SYSTEM (RAS)



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Critical

Acetylcysteine has been used in humans for decades for numerous indications. NAC is probably best known for its ability to rescue the liver from Paracetamol toxicity. It appears to be clinically important to rapidly get extremely high doses into the person to prevent free radical induced liver toxicity due to a metabolite.

Unfortunately, the above conditions that were used inappropriately in the next slide showing results from a double blind experiment designed to examine NAC for treating Covid symptoms.

Free radicals are signaling agents that are critical for many developmental decisions. In contrast, if they are excessively quenched they cannot trigger necessary developmental outcomes. Significantly lower doses of orally administered, shown to be effective for influenza H1N1 were not examined.

The effectiveness of this compound for respiratory issues is overwhelming. Results are clear, both in the peer reviewed literature and from, by many citizen scientists around the world. NAC inexpensive, highly effective treatment, yet been ignored by most medical practitioners in favor of vaccines and biologics that are completely unnecessary, especially when NAC is combined with agents that turn on fat burning such as CBD/THC and vitamin D

NAC is a well known therapeutic used to reverse liver toxicity.

It is sold over the counter in the United States, and much of the world

400 kg is on the way for Columbia and Ecuador

Hundreds of bottles of NAC/CBD capsules are currently successfully
in use by a variety of physicians

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Attenuation of influenza-like symptomatology and improvement of cell-mediated immunity with long-term N-acetylcysteine treatment.

S. De Flora, C. Grassi, L. Carati. ©ERS Journal Ltd 1997.

ABSTRACT: N-acetylcysteine (NAC), an analogue and precursor of reduced glutathione, has been **in clinical use for more than 30 yrs as a mucolytic drug**. It has also been proposed for and/or used in the therapy and/or prevention of several respiratory diseases and of diseases involving an oxidative stress, in general. The objective of the present study was to evaluate the effect of long-term treatment with NAC on influenza and influenza-like episodes.

A total of 262 subjects of both sexes (78% ≥ 65 yrs, and 62% suffering from non- respiratory chronic degenerative diseases) were enrolled in a randomized, double- blind trial involving 20 Italian Centres. They were randomized to receive either placebo or NAC tablets (600 mg) twice daily for 6 months. Patients suffering from chronic respiratory diseases were not eligible, to avoid possible confounding by an effect of NAC on respiratory symptoms.

NAC treatment was well tolerated and resulted in a significant decrease in the frequency of influenza-like episodes, severity, and length of time confined to bed. Both local and systemic symptoms were sharply and significantly reduced in the NAC group. Frequency of seroconversion towards A/H1N1 Singapore 6/86 influenza virus was similar in the two groups, but **only 25% of virus-infected subjects under NAC treatment developed a symptomatic form, versus 79% in the placebo group**. Evaluation of cell-mediated immunity showed a progressive, significant shift from anergy to normoergy following NAC treatment.

Administration of N-acetylcysteine during the winter, thus, appears to provide a significant attenuation of influenza and influenza-like episodes, especially in elderly high-risk individuals. N-acetylcysteine did not prevent A/H1N1 virus influenza infection but significantly reduced the incidence of clinically apparent disease. Eur Respir J 1997; 10: 1535–1541.

Expanded presentation of paper <http://canna-sapiens.com/scientific-papers/nac-1997-italian-study.pdf#previous-photo>

Rationale for the use of N-acetylcysteine in both prevention and adjuvant therapy of COVID-19

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Affiliations expand

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Free PMC article

Abstract

COVID-19 may cause pneumonia, acute respiratory distress syndrome, cardiovascular alterations, and multiple organ failure, which have been ascribed to a cytokine storm, a systemic inflammatory response, and an attack by the immune system. Moreover, an oxidative stress imbalance has been demonstrated to occur in COVID-19 patients. N-Acetyl-L-cysteine (NAC) is a precursor of reduced glutathione (GSH). Due to its tolerability, this pleiotropic drug has been proposed not only as a mucolytic agent, but also as a preventive/therapeutic agent in a variety of disorders involving GSH depletion and oxidative stress. At very high doses, NAC is also used as an antidote against paracetamol intoxication. Thiols block the angiotensin-converting enzyme 2 thereby hampering penetration of SARS-CoV-2 into cells. Based on a broad range of antioxidant and anti-inflammatory mechanisms, which are herein reviewed, the oral administration of NAC is likely to attenuate the risk of developing COVID-19, as it was previously demonstrated for influenza and influenza-like illnesses. **Moreover, high-dose intravenous NAC may be expected to play an adjuvant role in the treatment of severe COVID-19 cases and in the control of its lethal complications, also including pulmonary and cardiovascular adverse events.**

Keywords: COVID-19; N-acetyl-L-cysteine; glutathione; inflammation; oxidative stress.

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Curcumin is a plant product that has been used for centuries because of his medicinal value (anti-inflammatory, cancer diabetes, Alzheimer's). It turns on fat burning, cellular recycling a free radical damage components that are typically damaged when sugar burning is the main energy source. All living systems require energy to maintain the flow dependent living state. It is always maintained by movement into the future powered by carbohydrates and amino acids, while repair and reconstruction is driven by fast burning.

p53 is there an anti-cancer gene, a tumor suppressor. Most cancers burn carbohydrates. When sugar burning cancer cells burn fat, it disrupts cellular biochemical redox harmony sufficiently to cause apoptosis.

P53 is a tumor supressor gene. It turns on fat burning

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. 2020 Aug 31;e22616. doi: 10.1002/jbt.22616. Online ahead of print.

Curcumin induced apoptosis is mediated through oxidative stress in mutated p53 and wild type p53 colon adenocarcinoma cell lines

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PMID: 32864863 DOI: 10.1002/jbt.22616

Abstract

Curcumin has anti-oxidant, anti-cancer and anti-carcinogen property. Our laboratory had previously reported that, curcumin treatment induces reactive oxygen species (ROS) generation in HT-29 cell line, an effect contradictory to its anti-oxidant property. This study evaluates the role of p53 in curcumin mediated ROS generation and cell death. Curcumin induced ROS was determined by 2',7'-dichlorofluorescein and apoptosis by Hoechst33342/PI staining in HT-29 and HCT-116 cell lines. ROS generation occurs within 1 hour of 40 μ M curcumin treatment and a reduction was observed by third hour in HCT-116 insinuating p53 involvement. N-acetyl cysteine (NAC) pre-treatment effectively quenched ROS and inhibited membrane potential loss in HT-29, but less effective in HCT-116. Mitochondrial membrane potential loss is evident with 10 and 40 μ M curcumin in HCT-116 and at 40 μ M curcumin in HT-29. Total p53 protein level increase was observed by 24 hours in HCT-116 upon NAC pre-treatment. **Our results indicate that curcumin induces ROS mediated cell death in colon adenocarcinoma cell lines and may be mediated via p53**

Keywords: colorectal cancer; curcumin; p53; reactive oxygen species.

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P53 is a tumor supressor gene. It turns on fat burning

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The role of N-acetylcysteine in preventing hepatic injury associated with systemic oxidative stress after extracorporeal shock wave treatment.

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BACKGROUND: Systemic oxidative stress may cause detrimental consequences for the liver, leading to hepatic fibrogenesis. **OBJECTIVES:** To investigate histopathological changes in liver tissues due to the increased systemic oxidative stress associated with rat extracorporeal shock wave lithotripsy (SWL) model and to document the consequences of N-acetylcysteine (NAC) administration. **MATERIAL AND METHODS:** In this experimental SWL model, 18 Wistar albino rats were randomly assigned into 3 groups. The control group (group I) had no intervention. Group II underwent SWL treatment with intraperitoneal saline injection. Group III also had SWL with intraperitoneal NAC and was divided into short-term (group III-14 days) and long-term (group III-28 days) subgroup. Hepatectomy was performed for histopathological examinations. Histopathological alterations were evaluated with light microscopy. Immunohistological staining for p53 and myeloperoxidase was also performed. **RESULTS:** Blood samples revealed a significant increase in plasma oxidative stress index (OSI) after plasma total antioxidant status (TAS) and total oxidant status (TOS) had been measured. It was shown that this increased systemic oxidative stress adversely affected liver tissues. Predominantly, sinusoidal dilatation was remarkably observed in rats with significantly high OSI values ($p = 0.043$). Similarly, periportal necrosis significantly increased in rats with high OSI values ($p = 0.033$). p53 positivity was also remarkable in rats with systemic oxidative stress ($p = 0.049$). N-acetylcysteine administration provided a significant decrease in OSI. **N-acetylcysteine also improved all these alterations, including p53 staining. Particularly, sinusoidal dilatation was significantly protected in the long-term NAC group** (group III-28 days). **CONCLUSIONS:** We demonstrated that SWL-induced systemic oxidative stress causes histological alterations in liver tissues. Increased p53 and myeloperoxidase staining as markers of oxidative damage were also detected. N-acetylcysteine may protect from these histological and ultra-structural alterations related to oxidative stress.

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Bisphenol A the plasticizer contaminant that everyone is exposed to. It has hormone like activity, promotes cancer, does not promote health.

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Antioxidants (Basel) 2019 Oct 21. 8:10.3390/antiox8100497

N-Acetylcysteine Attenuates the Increasing Severity of Distant Organ Liver Dysfunction after Acute Kidney Injury in Rats Exposed to Bisphenol A.

Peerapanyasut, W, Kobroob, A, Palee, S, Chattipakorn, N, Wongmekiat, O

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Distant organ liver damage after acute kidney injury (AKI) remains a serious clinical setting with high mortality. This undesirable outcome may be due to some hidden factors that can intensify the consequences of AKI. Exposure to bisphenol A (BPA), a universal chemical used in plastics industry, is currently unavoidable and can be harmful to the liver. This study explored whether BPA exposure could be a causative factor that increase severity of remote liver injury after AKI and examined the preventive benefit by N-acetylcysteine (NAC) in this complex condition. Male Wistar rats were given vehicle, BPA, or BPA + NAC for 5 weeks then underwent 45 min renal ischemia followed by 24 h reperfusion (RIR), a group of vehicle-sham-control was also included. RIR not only induced AKI but produced liver injury, triggered systemic oxidative stress as well as inflammation, which increasing severity upon exposure to BPA. Given NAC to BPA-exposed rats diminished the added-on effects of BPA on liver functional impairment, oxidative stress, inflammation, and apoptosis caused by AKI. NAC also mitigated the abnormalities in mitochondrial functions, dynamics, mitophagy, and ultrastructure of the liver by improving the mitochondrial homeostasis regulatory signaling AMPK-PGC-1 α -SIRT3. **The study demonstrates that NAC is an effective adjunct for preserving mitochondrial homeostasis and reducing remote effects of AKI in environments where BPA exposure is vulnerable.**

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Anecdotal reports, from numerous people, unambiguously show profound benefits for using a combination of CBD and NAC to dramatically benefit patients suffering from COPD and asthma. No statistics needed the results are obvious to anyone using it. The same combination has a very dramatic positive affect on Covid and other viral respiratory infections. NAC directly quenches the dangerous excess free radicals that lead to cell death, while at the same time the CBD turns on fat burning that turns off the carbohydrate metabolism required for the virus infection to proceed.

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Int J Chron Obstruct Pulmon Dis 2015. 10:917-23. 10.2147/COPD.S79710

Effect of N-acetylcysteine in COPD patients with different microsomal epoxide hydrolase genotypes.

Zhang, JQ, Zhang, JQ, Liu, H, Zhao, ZH, Fang, LZ, Liu, L, Fu, WP, Shu, JK, Feng, JG, Dai, LM

Department of Respiratory Critical Care Medicine, First Affiliated Hospital of Kunming Medical University, Kunming, People's Republic of China.

BACKGROUND: The role of the antioxidant N-acetylcysteine (NAC) in the treatment of chronic obstructive pulmonary disease (COPD) has not been clarified as yet. In early studies, we found that the proportion of smokers with COPD having extremely slow/slow microsomal epoxide hydrolase (EPHX1) enzyme activity is significantly higher than that in healthy smokers. The purpose of this study was to evaluate whether different EPHX1 enzyme activity is related to differential therapeutic effects of treatment with NAC in COPD. **METHODS:** A total of 219 patients with COPD were randomly allocated to an extremely slow/slow EPHX1 enzyme activity group (n=157) or a fast/normal EPHX1 enzyme activity group (n=62) according to their EPHX1 enzyme activity. Both groups were treated with NAC 600 mg twice daily for one year. The main study parameters, including forced expiratory volume in one second (FEV1), St George's Respiratory Questionnaire (SGRQ), and yearly exacerbation rate, were measured at baseline and at 6-month intervals for one year. **RESULTS:** Both FEV1 and SGRQ symptom scores were improved after treatment with NAC in the slow activity group when compared with the fast activity group. Further, changes in FEV1 and SGRQ symptom score in patients with mild-to-moderate COPD were more significant than those in patients with severe-to-very severe COPD. The yearly exacerbation rates were reduced in both groups, but the reduction in the slow activity group was significantly lower than in the fast activity group. **CONCLUSION:** NAC treatment in COPD patients with extremely slow/slow EPHX1 enzyme activity improves FEV1 and the SGRQ symptom score, especially in those with mild-to-moderate COPD, and polymorphism in the EPHX1 gene may have a significant role in differential responses to treatment with NAC in patients with COPD.

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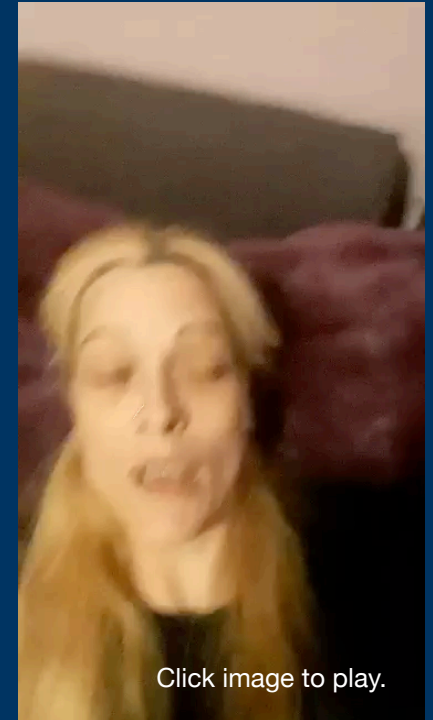
Metabolic Manipulation

This woman was born prematurely, spent first month of life in incubator, consequently her lungs were underdeveloped, and she suffered asthma/COPD/severe allergies her entire life, after have spent her first month of life incubated.

A few years ago we discovered that the combination of NAC and CBD controlled her respiratory problems to such a degree that she forgot she had them.

Unfortunately, due to Covid restrictions, multiple shipments totaling 3 kg of NAC we're delayed. NAC is not readily available in Serbia and she had run out for three days before her allergies hit overwhelmed her, even with CBD.

Two months later, while taking THC/CBD, vitamin D and NAC, she developed all the Covid symptoms, but in a completely inconsequential fashion.



Translation
"I am dying. Please pray for me"

The combination of NAC, CBD and vitamin D can quickly, safely and rapidly end the pandemic

As President Trumps has said “It will just go away”, “What do you have to lose”?

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