Case Report 1: NAD+ Oscillation Therapy (NOT) to treat Covid-19 aggravated by poorly controlled Diabetes Melitus Type 2

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Case Report

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Abstract

We report on a case of a 50 year old diabetic, obese and hypertensive male patient that developed severe disease, was admitted and treated with NAD+ Oscillation Therapy (NOT) and then discharged in a stable condition within 5 days (not requiring home oxygen therapy). In addition to the favourable outcome in regards to severe COVID-19 disease, the patient's blood glucose levels were better controlled after resolution of COVID-19 and the patient has no apparent post-COVID-19 morbidity, which has been reported in countries across the world.

NAD+ Oscillation Therapy is a novel medical treatment developed in South Africa. NAD Oscillation Therapy envelops the real time measurement of the NAD+/NADH ratio and modulation of the ratio with the goal of restoration of homeostasis. This supports the primary role of the immune system which is protection and restoration.

This case shows a favourable treatment outcome in a high risk patient that developed severe disease. Treatment was initiated early and hospitalization was done before laboratory markers reached critical levels. This case highlights the importance of early treatment initiation, effective patient counselling re home care (recognition of sepsis and respiratory distress), NOT as a realtime treatment method of sepsis and the advantage of NOT as a treatment modality in COVID-19 patient care.

Abbreviations

BMI - Body Mass Index
COVID-19 - Corona Viral Disease 2019
CRP - C-Reactive Protein
DMT2 - Diabetes Mellitus Type 2
IV - Intravenous
LDH - Lactate Dehydrogenase
NAD+ - Nicotinamide Adenine Dinucleotide
NADH - Reduced Nicotinamide Adenine Dinucleotide
NLR - Neutrophil-Lymphocyte Ratio
NOT - NAD+ Oscillation Therapy

Background

There is an emerging concept that changes in cellular bioenergetics concomitantly reprogram inflammatory and metabolic responses (1,2). A metabolic polarity exists between the anabolic proinflammatory phase, which requires glycolysis to meet the rapid demands for high energy during the early response to a threat, and the catabolic adaptation phase, which depends on fatty acid oxidation to heal and restore homeostasis (1). With current research it is becoming more apparent that Diabetes Mellitus Type 2 is a multi-etiological disease that shows dysfunction of energy metabolism on a cellular level (3).

Diabetes Mellitus Type 2 is an independent risk factor for increased mortality in COVID-19 patients. Previous research shows that patients with Diabetes Mellitus Type 2 and/or uncontrolled hyperglycemia had longer hospital stays and higher mortality rates. It has also been shown from previous research that patients with 2-3 comorbidities were more likely to die. HbA1c is associated with inflammation, hypercoagulability, and low SaO2 in COVID-19 patients, and the mortality rate is higher in diabetic patients (4). Patients with diabetes and/or hyperglycemia had higher mortality rates with COVID-19 than non-diabetic patients and those with normoglycemia. The length of hospital stay was also longer in patients with hyperglycemia (5). Well controlled blood glucose levels was associated with reduced mortality and reduced length of hospital stay (6).

We present a novel, multimodal treatment approach, named NAD+ Oscillation Therapy (NOT) to actively treat a COVID-19 patient in sepsis aggravated by poorly controlled Diabetes Mellitus Type 2 (DMT2).

Case Presentation

50 year old male patient first presented on 20/06/2020 with symptoms of mild disease. Admitted on 22/06/2020 with dyspnoea. Discharged on 26/06/2020 in stable condition not requiring Oxygen. 10 July 2020: SARS-CoV-2 PCR not detected.
Risk factors:

- Poorly controlled Diabetes Mellitus Type 2 on insulin.
    - HbA1c = 8.2% (30/04/202) with self reported fasting blood glucose measurements of 14.8-16.4 mmol/L.
- Untreated Hypertension:
    - 07/03/2020: BP 146/97 mmHg (patient never returned for follow up).
    - 20/06/2020: BP 152/90 mmHg.
- Obesity
    - BMI = 32.9

First presentation on Day 3 of disease onset

Initial presenting symptoms: Sore throat and loss of taste and smell for 3 days followed by coughing and mild exertional dyspnoea. No fever.
Clinical presentation: Temperature 37.3 OC; Pulse rate 91 bpm; Oxygen saturation 96% (room air); Blood Pressure 152/90 mmHg.
Special investigations (24hr delay for results):

- SARS-CoV-2 PCR: Detected.
- Lymphocyte %: 18%
- Neutrophil/Lymphocyte ratio: 4.1
- Lactate Dehydrogenase: 274
- C-Reactive Protein: 75
- D-Dimer: 0.48
- Ferritin: 462.3
- NAD+/NADH = 90/10

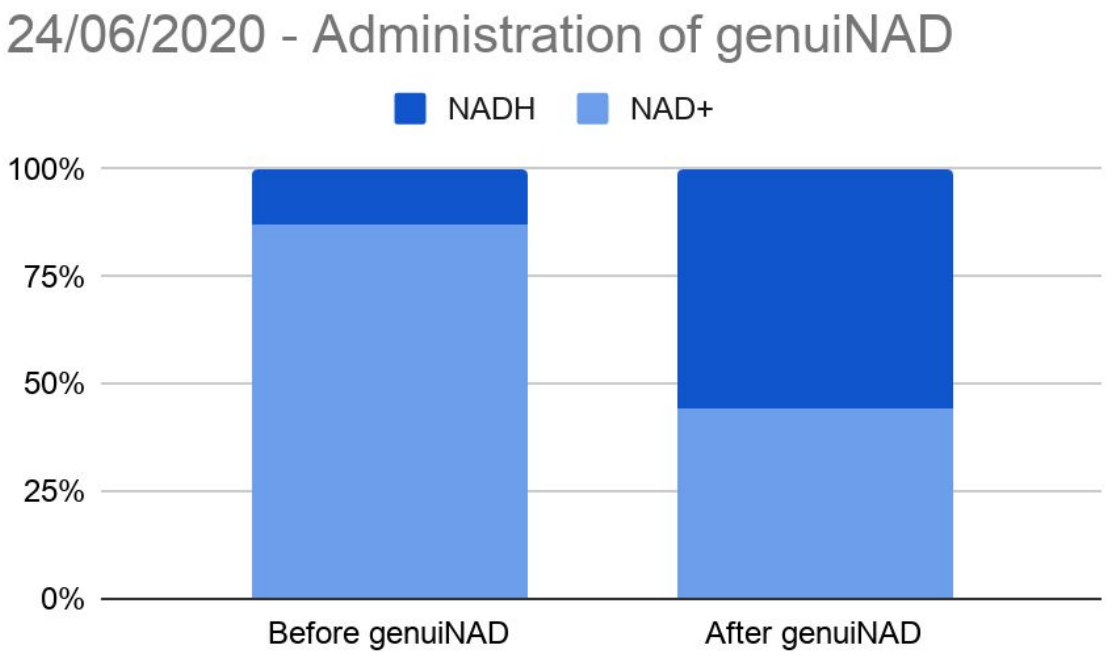
Elevated Ferritin, LDH, CRP and decreased Lymphocyte percentage (elevated NLR) all have prognostic value for severe disease and mortality. According to CDC classification this case is classified as severe disease (5).

Treatment (while awaiting results):

- NAD+Phyto 3 capsules tds po
- Anadin 1 qid po
- Benylin Original 10ml q4h (maximum 4 times per day) - Active ingredient Ammonium Chloride.

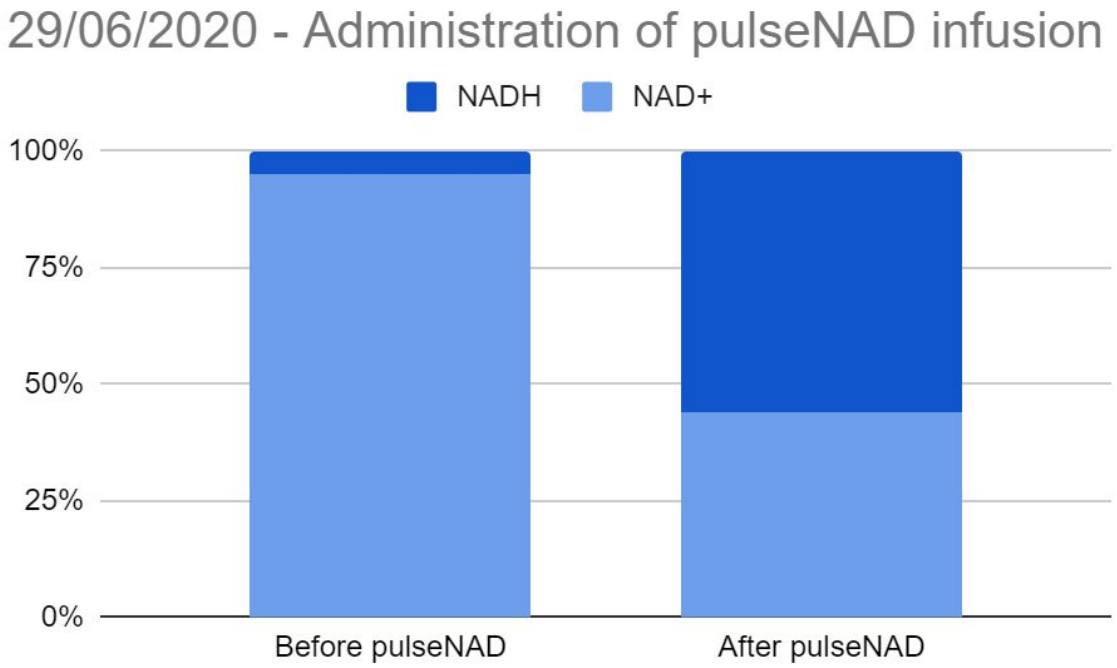
Progression of COVID-19

22/06/2020: Clinically deterioration. Self reported respiratory rate increased to 30 breaths per minute and the patient was advised to be admitted. Considering the date of onset of symptoms we calculated disease duration as day 7, which is the median time to admission from reported cases (6). Improvement noted on NLR and Total Lymphocyte % from initial prognostic markers. Peptamen was started as nutritional support with specific focus on medium chain triglycerides as energy source for the immune system.
24/06/2020: Treatment: GenuiNAD IV Treatment administered. Improvement in saturation and symptoms observed within 24 hours. Laboratory markers started normalising. Targeted treatment outcome achieved. See Graph 1.



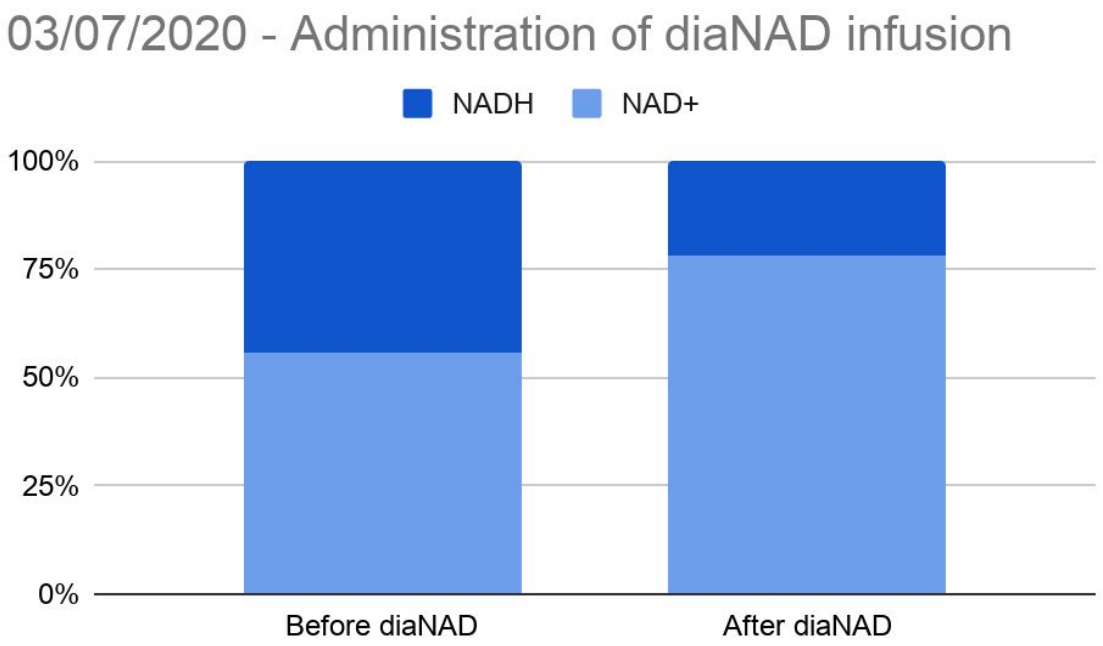
Graph 1 - NAD+/NADH ratio before and after genuiNAD. The aim is to modulate the adaptation phase of the immune response by normalizing the NAD+/NADH ratio to 50/50. NAD+/NADH Before = 87/13 After 44/56

26/06/2020: Patient discharged. Maintains sp02 > 92% on room air. CRP = 14,7. D-Dimer 0.53.
29/06/2020: Patient follow up outpatient. Patient stable. NAD+/NADH = 95/5. Still in hypoinflammatory/adaptation phase of immune response. Treatment: pulseNAD IV infusion.



Graph 2 - NAD+/NADH ratio before and after pulseNAD. The aim is to modulate the adaptation phase of the immune response by normalizing the NAD+/NADH ratio to 50/50. NAD+/NADH Before = 87/13 After 44/56

03/07/2020: Return to homeostasis. Patient stable, no complaints. Treatment complemented by self reported Blood glucose measurements ranging 6-8mmol/L. Much improved from pre-COVID-19 measurements. NAD+/NADH = 56/44. Treatment: DiaNAD IV infusion. Aim to stimulate the mending pathways through elevation of the NAD+/NADH.



Graph 3 - NAD+/NADH ratio before and after diaNAD. The aim is to modulate NAD+/NADH ratio to improve the management of Diabetes Mellitus Type 2. NAD+/NADH Before = 56/44 After 78/22.

Radiology:

Hospital Radiologist Report

Chest X-Rays Report (23 June 2020):

Bilateral patchy and striated groundglass opacity more prominent right lung and left lower lobe. Bilateral lower lobe atelectasis.

Chest X-Rays Report (26 June 2020):

Perihilar bronchial cuffing and tram tracking is suggestive of bronchitis. No discrete consolidation or groundglass opacity to suggest a fulminant Lower respiratory tract infection or COVID-19.

Independent Radiologist Report

1 st Chest Radiograph on 23 June 2020;

Technique AP portable of the chest.
Impression: There is a suboptimal inspiratory effort. There is differential transradiancy with the right lung demonstrating confluent ground glass opacification. In addition, there are bilateral lower and mid zone patchy areas of atelectasis and consolidation. Bilateral

bronchial wall thickening is present. There are no pleural effusions and no pneumothorax. The vascular pedicle and mediastinal silhouette is normal with no cardiomegaly. No significant upper lobe blood diversion.

Follow up chest Radiograph on 26 June 2020:

Technique: AP portable of the chest.
Impression: in comparison to the previous Radiograph there is an improved inspiratory effort. There is reduced bilateral mid and lower zone patchy areas of consolidation. The previously described bronchial wall thickening is persistent. The right lung ground glass opacification has resolved. The remainder of the findings are unchanged with no new findings.

Comment:

The biggest technical factor which could potentially influence interpretation of this series of Radiograph is the poor inspiratory effort on the initial chest Radiograph. Poor inspiratory effort could demonstrate patchy areas of consolidation and atelectasis of the mid and lower zones without any underlying pathology. Nevertheless, the ground glass opacification is unlikely the result of poor inspiration, due to the marked asymmetry. The differential diagnosis for this would include viral pneumonia, including Covid 19 Respiratory related disease, pneumocystis pneumonia, acute Respiratory distress syndrome (Ards), pulmonary oedema of interstitial lung disease with interim improvement.

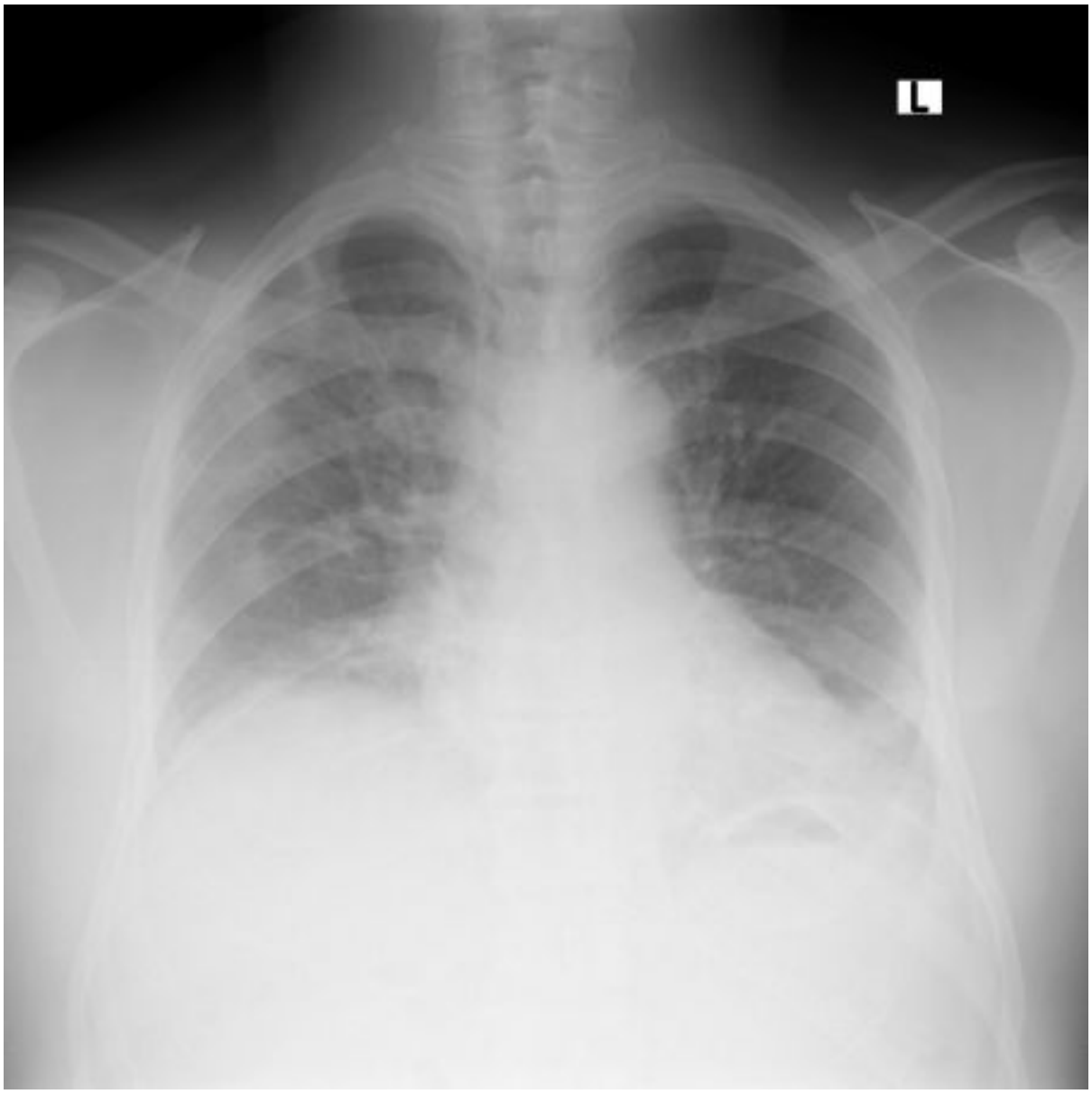


Figure 1 - Chest X-Rays Report (23 June 2020): Bilateral patchy and striated groundglass opacity more prominent right lung and left lower lobe. Bilateral lower lobe atelectasis.

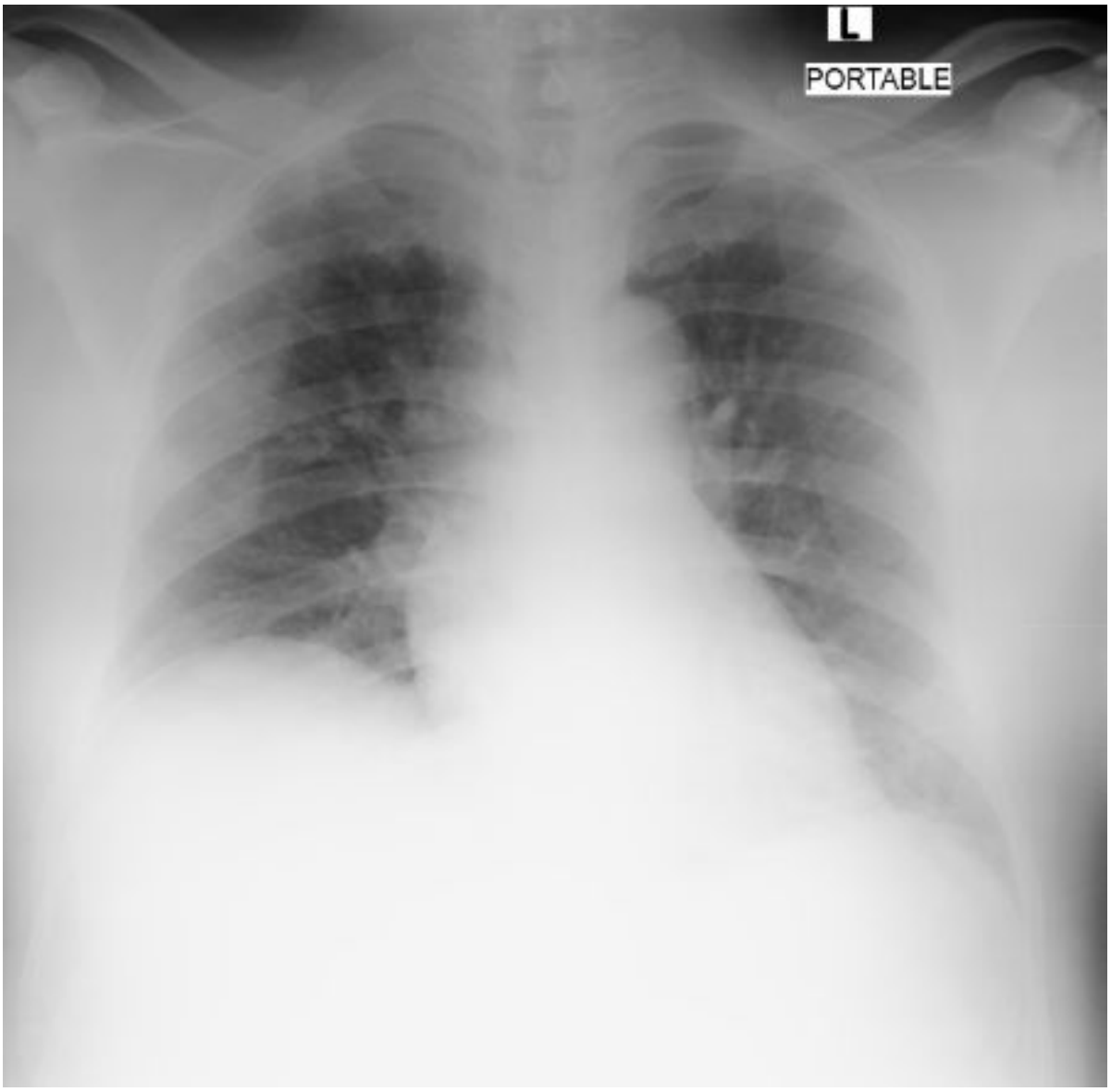


Figure 2 - Chest X-Rays Report (26 June 2020): Perihilar bronchial cuffing and tram tracking is suggestive of bronchitis. No discrete consolidation or groundglass opacity to suggest a fulminant Lower respiratory tract infection or COVID-19.

Treatment	Date Started	Duration
Anadin 1 qid po	20/06/2020	Until 22/06/2020
NAD+Phyto 3 tds po	20/06/2020	Continue
Benylin Original 10ml tds po	20/06/2020	Until 03/07/2020
Clexane S/C 40IU nocte	23/06/2020	Two weeks after discharge
Anadin 1 daily mane po	23/06/2020	Continue
Peptamen	23/06/2020	Two weeks after discharge

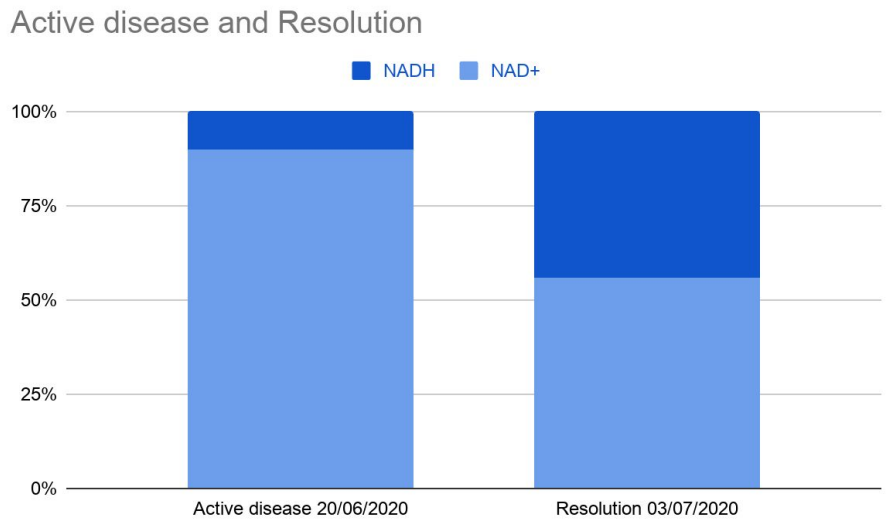
genuiNAD drip	24/06/2020	2 hours
Fluoxetine 20mg daily mane	25/06/2020	14 days
pulseNAD drip	29/06/2020	Over 2 hours
diaNAD drip	03/07/2020	Over 2 hours

Table 1 - Treatments

Date	20/06/2020	22/06/2020	23/06/2020	24/06/2020	25/06/2020	26/06/2020
D-Dimer	0.48	0.62	0.69	0.55	0.61	0.53
CRP	75	104	101.9	72.9	32.7	14.7
LDH	274	328	237	265	239	200
Ferritin	462.3	558		649.3	640.2	
SARS-CoV-2	Detected					
IL-6				5.4		
WCC	5.7	6.6	6.9	5	4.6	6.5
Neu	4.22	3.95	4.55	3.2	2.8	4.19
Lym	1.03	2.05	1.93	1.3	1.2	1.63
Eosino		0.05		0.1	0.1	0.14
Platelets	210	239	250	327	355	412
Lym %	18	31.1	28	25.7	26	25.3
Neu/Lym Ratio	4.10	1.93	2.36	2.46	2.33	2.57
ESR	40	40		98		

Table 2 - Laboratory special investigations

Resolution of Adaptation Immune Response

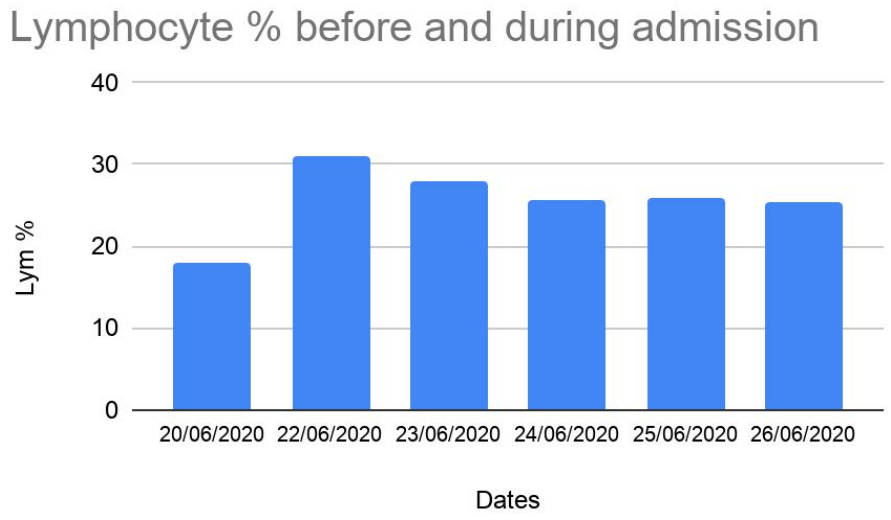


Graph 4 - Resolution of the adaptation / hypoinflammatory phase of the immune response. NAD+/NADH ratio indicates return to homeostasis.

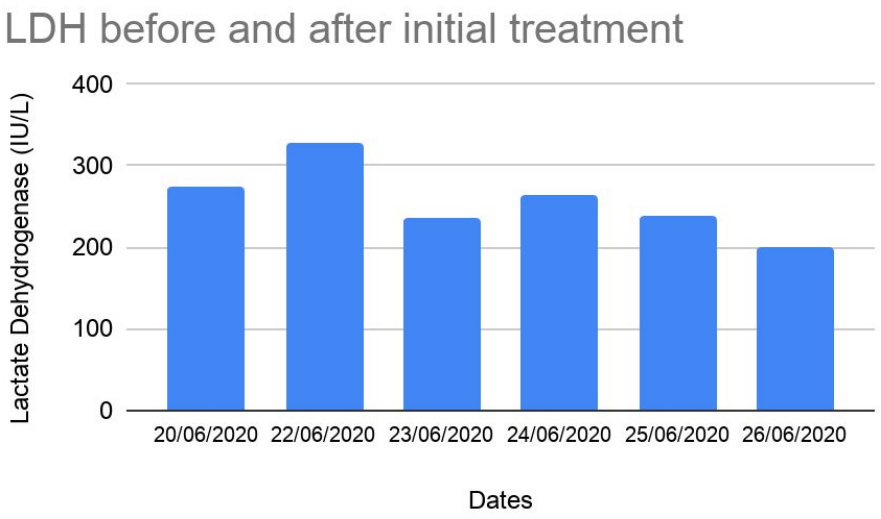
Unique accomplishments in treatment

Laboratory Markers

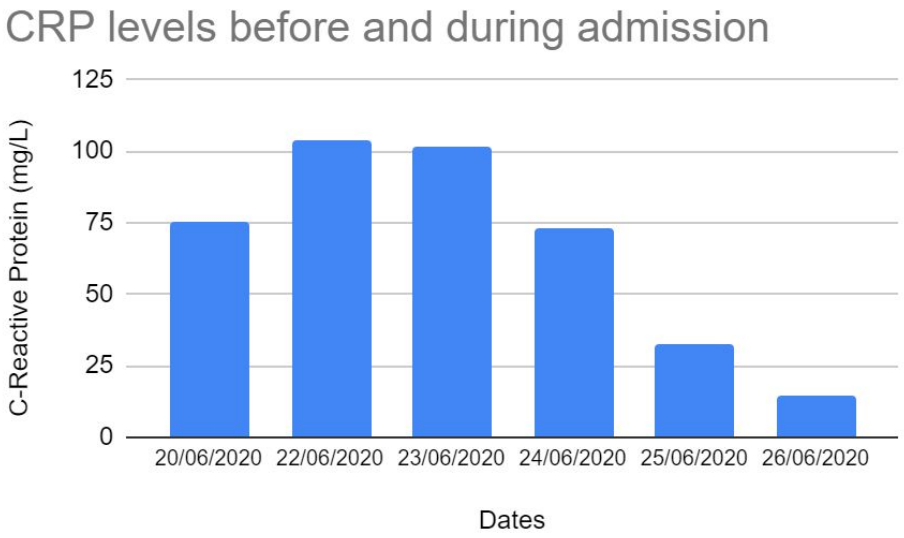
Treatment started on 20/06/2020 before COVID-19 was confirmed with nutritional support (NAD+Phyto), Anadin and Benylin Original. His Total Lymphocyte % increased over 2 days and remained stable for the duration of admission. LDH peaked on 22/06/2020 and steadily decreased during the 5 days of admission. CRP peaked on 22/06/2020, started decreasing after admission and rapidly dropped after genuiNAD IV treatment on 24/06/2020. This coincided with a reduced need for oxygen from 24/06/2020.



Graph 5 - Lymphocyte % before and during admission



Graph 6 - Normalisation of LDH levels.



Graph 7 - C-Reactive Protein levels decreased indicating decreased inflammation.

Radiology

Two chest X-rays was taken 3 days apart and a rapid improvement was noted. The patient's need for oxygen decreased from 10L/min on 22/06/2020 to being not dependent on oxygen on 26/06/2020. This coincided with improvement in laboratory markers.

Discussion

Inflammation is an evolutionarily conserved, coordinated response to harmful stimuli, with a goal of returning to homeostasis (1,7). The inflammatory response has a unifying purpose encoded in the germline: protection and restoration. (1) The components of the innate and

adaptive immunity fulfill this purpose, during which a typical inflammatory response progresses from a proinflammatory to an adaptive phase and eventually restores homeostasis. (1)

There is an emerging concept that changes in cellular bioenergetics concomitantly reprogram inflammatory and metabolic responses (1,2). A metabolic polarity exists between the anabolic proinflammatory phase, which requires glycolysis to meet the rapid demands for high energy during the early response to a threat, and the catabolic adaptation phase, which depends on fatty acid oxidation to heal and restore homeostasis (1).

The fuel switch between the anabolic proinflammatory phase to the catabolic adaptation phase of the immune response depends on the sensing of AMP and NAD+ by AMPK and the SirT family of deacetylases (e.g. SIRT1, -6 and-3). These sequential steps of the AMP-AMPK/NAD+ -SirT axis are just as relevant to the inflammatory responses seen with COVID-19 as it is to all immune responses. The immune response correlates well with the disease progression of COVID-19. In our case reports we have monitored the NAD+/NADH ratio from diagnosis, through treatment and up to resolution of disease. Modulation of the NAD+/NADH ratio was also achieved through targeted treatment of the NAD+/NADH ratio.

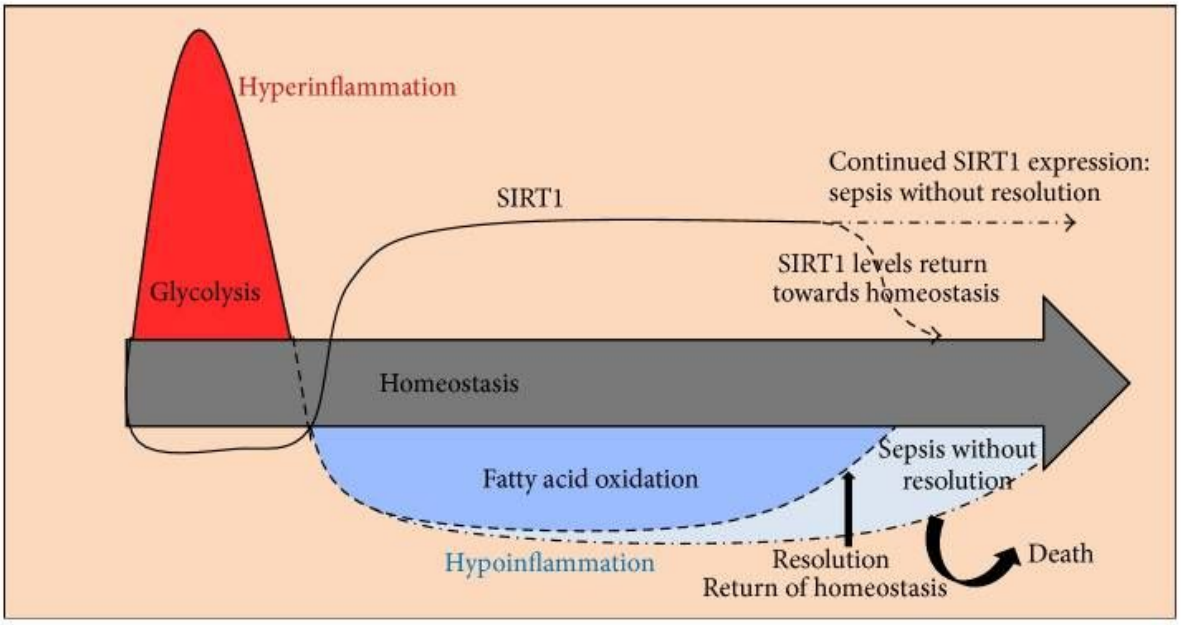


Figure 3. Sirtuins and acute inflammation of sepsis: the extreme stress response of sepsis rapidly induces a systemic and potentially lethal hyperinflammatory state (red), which shifts within hours to a counterreactive hypoinflammation/adaptation phase (blue). NAD+ activation of sirtuins directs this switch. Mechanistically, nuclear SIRT1 levels briefly drop when homeostasis deviation initiates the glycolysis-dependent hyperinflammation, but within hours nuclear and mitochondrial sirtuin activation shifts glycolysis to fatty acid oxidation. This metabolic reprogramming globally represses immunity, affecting neutrophils, monocytes, dendritic cells, NK cells, and T lymphocytes. Resolution of acute inflammation and sepsis rebalances sirtuins and inflammation to restore homeostasis. Persistent elevation of sirtuins and hypoinflammation as a result lead to death (denoted by light blue area).(2)

Current research on NAD+, Sirtuins, inflammation and phytonutrients allows for modulation of the immune response through therapies targeted at upregulating and downregulating the NAD+/NADH ratio. The aim is to use low-risk, cost effective therapies to oscillate the

bioenergetics through the NAD+/NADH ratio. This therapy is hereby termed NAD+ Oscillation Therapy (NOT) with the sole purpose of rebalancing cellular bioenergetics. NAD+ Oscillation Therapy includes:

1. Testing the NAD+/NADH ratio to guide treatment.
2. Modulating the NAD+/NADH ratio to achieve desired outcomes.
3. Enabling oscillation of bioenergetics to resolve disease states.

Previous research on Nicotinamide adenine dinucleotide (NAD), Sirtuins and the NAD+/NADH ratio in Diabetes Mellitus Type 2 is well documented and it is becoming more apparent that Diabetes Mellitus Type 2 is a multi-etiological disease that shows dysfunction of energy metabolism on a cellular level (3). This dysfunction in cellular metabolism on a systems level, together with COVID-19, increases the risk of severe disease and mortality. The immune system becomes less responsive to injury and the necessary immune response does not happen (see figure 4 and 5).

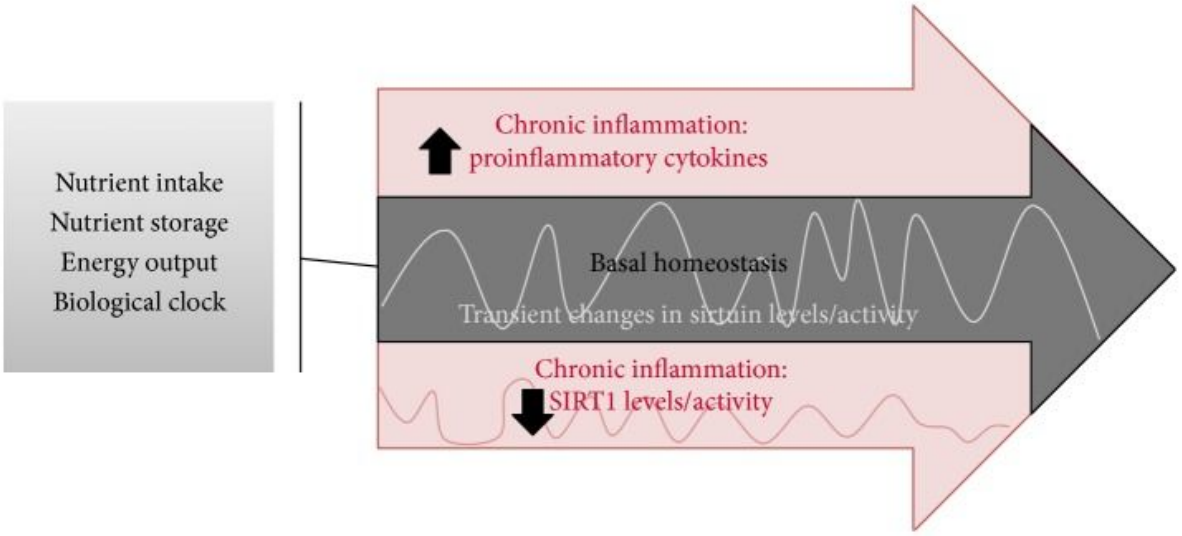


Figure 4. Sirtuins and chronic inflammation: during homeostasis (grey arrow), there are small perturbations in sirtuin levels without inflammation. During chronic inflammatory states (denoted by pink), persistent decreases in SIRT1 levels/activity sustain glycolysis-dependent proinflammatory pathways. This immunometabolic inflexibility alters the bioenergy homeostasis set point, which is rebalanced by increasing SIRT1 activity (2)

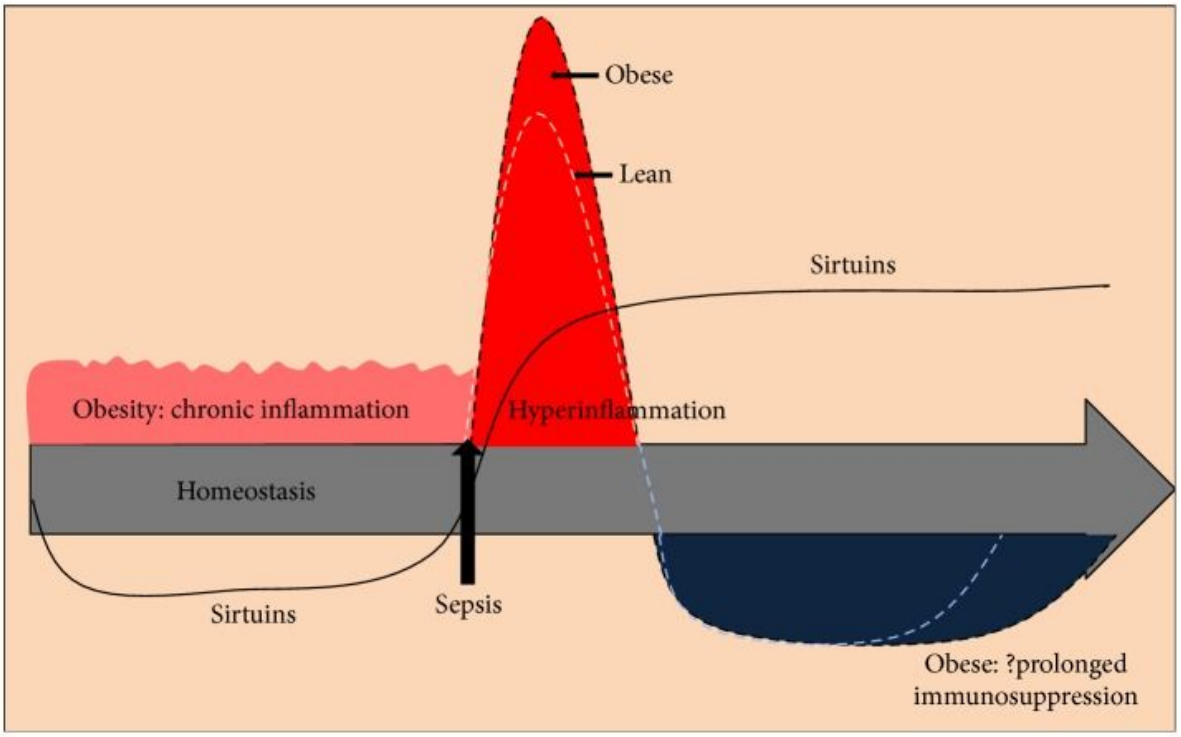


Figure 5. Sirtuins and obesity with sepsis: obesity is associated with low-sirtuin levels/activity, but mechanisms responsible for this imbalance are unknown. If sepsis occurs in obese individuals with low SIRT1, the early hyperinflammatory phase is accentuated and counteractive adaptation stage may be prolonged. Activating SIRT1 before obesity-associated sepsis prevents the accentuated acute inflammatory reaction. (2)

NAD+ Oscillation Therapy in COVID-19

The aim of treatment is to diagnose COVID-19 early, do risk assessment early and treat high risk cases aggressively with a multimodal approach. To achieve this goal a fast, realtime test is needed, which we find in the NAD+/NADH Analyser. The NAD+/NADH Analyser was developed by Theo Verwey in the search for a cost effective and fast NAD+/NADH ratio calculation. The calculation is based on the Lactate/Pyruvate ratio, but has been improvised to use glucose instead of pyruvate. Pyruvate measurement is expensive and results are not readily available. Capillary glucose measurements are readily available and results are available within seconds. Point of Care Lactate measurements are also readily available and numerous devices are available. The glucose and lactate is measured on one drop of blood on both the left and right fingers.

Measurement

Use of NAD+/NADH Analyser

The NAD+/NADH analyser is a calculator used for estimating the NAD+/NADH ratio.
Inputs (Tests done with the ROCHE Accutrend Plus device):

- Bilateral capillary lactate level.

- Bilateral capillary glucose level.

These results are sent for calculation of the NAD+/NADH ratio with a proprietary calculator.
Notes on the NAD+/NADH ratio:

1. The total NAD Pool of 3 grams (strictly regulated) is reflected as 100 and consists of various organ and tissue related NAD subpools. For example, the stomach and intestines account for 37% and the muscles for only 1% of the total NAD Pool.
2. The total NAD Pool is mainly made up as follows:
   2.1 NAD+ and NADH = 62%
   2.2 NADP+ and NADPH = 38%
3. NADH, NADP+ and NADPH are derivatives of NAD+.
4. The NAD+/NADH ratio reflects the total oxidised NAD (NAD+ plus NADP+) and total reduced NAD (NADH plus NADPH) levels. The normal NAD+/NADH ratio will be 50/50
5. Only in exceptional cases, for example cancer, will the total NAD+ Pool of 3 grams be exceeded.
6. The NAD+/NADH ratio is the highest between 06h30 and 20h30 and the lowest between 20h30 and 06h30. The NAD+/NADH ratio is mainly restored between 20h30 and 06h30.
7. The aim of NAD+ Oscillation Therapy is to normalise the NAD/NADH ratio to function at the 50/50 ratio and restore homeostasis.

Determine disease phase

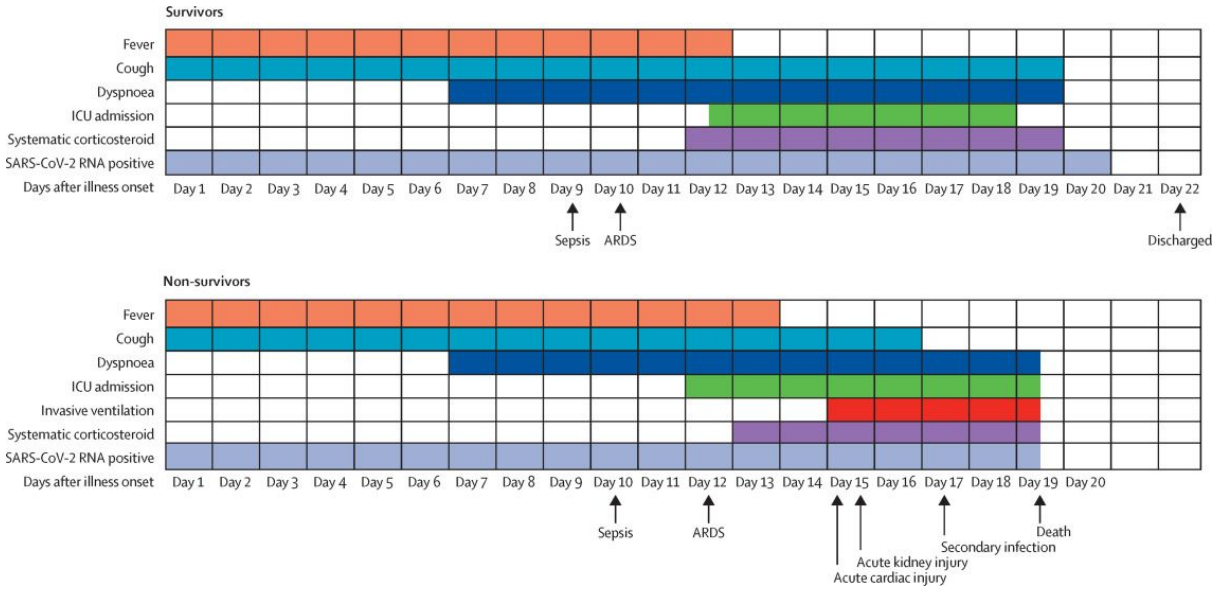
The NAD+/NADH ratio at homeostasis should be 50/50. Pre-existing NAD+/NADH ratios correlate well with disease outcomes. Previous research has shown that chronically low Sirtuin levels (and NAD+/NADH ratio) are strongly associated with chronic inflammation (1,2). Pre-existing NAD+/NADH ratio should be calculated for risk assessment.

Healthy vs Unhealthy immune response

The expected healthy immune response to COVID-19 is a hyperinflammatory response that lasts for hours to a few days which is followed by the adaptation phase. The initial drop in the Sirtuin level (NAD+/NADH ratio) is missed and most patients will present early in the adaptation phase or in the bridging phase. When checked against the duration of disease the disease phase can be determined. The NAD+/NADH ratio can be used to track disease progression and to determine resolution of the immune response and a return to homeostasis.

Chronic inflammatory conditions have a suppressed immune system and the immune response will be totally inadequate. The eventual hyperinflammatory response will be robust and exceed the normal hyperinflammatory response. These patients will either present in the pre-hyperinflammatory phase, complaining of mild symptoms, or in the hyperinflammatory phase when they present with severe disease. The ensuing hypoinflammatory phase will be dysregulated and if no appropriate intervention is applied lead to death.

The NAD+/NADH ratio can be used to determine whether the immune response matches the expected change in the NAD+/NADH ratio which correlates with the Sirtuin levels. For instance, a patient that presents on day 7 of disease with a low NAD+/NADH ratio probably has a dysregulated immune response which signifies possible severe disease progression. Similarly a patient with a continued high NAD+/NADH ratio may show unresolved hypoinflammation which again carries a poor prognosis. The NAD+/NADH ratio should be modulated to return to homeostasis to improve outcomes. During NOT the NAD+/NADH ratio is purposefully suppressed or elevated to stimulate NAD+/NADH oscillation and eventually restore homeostasis. The NAD+/NADH analyzer is an affordable, point of care test that is used to guide treatment decisions on a real time basis. It serves as a decision support tool for interventions, like antibiotic or immunosuppressive therapies. It can also be used to measure the immune response to immunizations.



Clinical courses of major symptoms and outcomes and duration of viral shedding from illness onset in patients hospitalised with COVID-19 - Figure shows median duration of symptoms and onset of complications and outcomes. ICU=intensive care unit. SARS-CoV-2=severe acute respiratory syndrome coronavirus 2. ARDS=acute respiratory distress syndrome. COVID-19=coronavirus disease 2019.(14)

Measure treatment response

Specific interventions will affect the NAD+/NADH ratio and NAD+ Oscillation Therapy is the science of appropriately using targeted pulse treatments to achieve desired outcomes. NAD+/NADH oscillation during homeostasis depends on nutrient intake, nutrient storage, the biological clock and energy output.

Intravenous infusions have been developed with established compounds to achieve such outcomes. The immune system is modulated through cellular metabolism and modulation of the NAD+/NADH ratio. A quick point of care test before and after the intervention determines treatment effect.

Treatment

Phytonutrients

NAD+Phyto has been formulated as a medical foods product that restores and normalises the NAD+/NADH ratio. Good nutrition is essential for a healthy immune response to infection and or sepsis. It is a plant based product.

Targeted interventions to modulate the NAD+/NADH ratio

Established drugs and compounds were repurposed to treat specific aspects of COVID-19.

Oral treatments

Anadin

Aspirin recycles NAD+ and increases the NAD+/NADH ratio. Its metabolism also results in catechol.

Peptamen

Nutritional support. Medium chain triglycerides act as the main energy source for the leukocytes and heart muscle cells.

Fluoxetine

Fluoxetine inhibits SARS-CoV-2 viral expression. Fluoxetine is an amphiphilic molecule (7). Fluoxetine is a safe drug that has been used for depression for many years. Short term use during SARS-CoV-2 infection is a low risk option that is effective. Fluoxetine further improves the patient's mood during disease and decreases anxiety.

Intravenous treatments

Established compounds repurposed to treat COVID-19. GenuiNAD, PulseNAD and DiaNAD are IV formulations specifically designed to modulate the NAD+/NADH ratio and the immune system.

Conclusion

NAD Oscillation Therapy (NOT) is the treatment method that was followed to treat COVID-19. We present this case study to show the advantage of using the NAD+/NADH Analyzer to guide treatment decisions and use existing drugs repurposed to treat COVID-19 and modulate the immune response. Independent research on NAD, sirtuins and inflammatory pathways provided the framework to connect the dots and find a solution for COVID-19 and possibly sepsis.

Patient perspective

On Thursday 18th June 2020 I started feeling very cold. I could not work out what was going on. The next evening I started coughing, feeling tired and developed a headache. This was dreadful. It felt like someone was blowing up my head like you would blow up a balloon. The next day I went to Dr X. He did the test to determine my NAD levels. He said that it appeared to him that there were signs of Covid. I was so scared. The Laboratory also took my tests and I got my results on Sunday evening which confirmed that I tested positive.
From Monday to Wednesday were the worst days of my life. I could not breathe. I was on oxygen. I even struggled to walk from my bed to the toilet which was not far away. My feet could not take the weight of my body. My body was in pain and I could not breathe properly. The breathing was the most painful thing I've ever had in my life.

Dr X took care of me. He told me about the NAD+Phyto tablets and I started taking it – up to 9 a day. I also took Benylin Original and Anadin and something else. He gave me a drip on Wednesday and on Thursday I could feel that things started to change. My body started feeling better. On Friday I was discharged.

After being discharged my wife drove me to the surgery. I was sitting in the back and the weirdest thing happened to me. I could not handle it to sit in a moving object. It felt like I've never driven in a car before. I was sweating, sweating!

My recovery was very difficult, because you are out of the doctor's care and continue on your own. I coughed blood around 14 times during this difficult time of recovery. Every morning I woke up at around 7h30. By 11h00 my body was so tired that I went back to sleep again until 16h00. Then by 20h00 I fell asleep again. My body was just so tired.
For 4 days after being released I could not feel whether it was hot or cold. My body could not determine the temperature. Only by day 5 could I feel that it was actually cold and I wanted extra jackets. There was still a heavy load sitting on my chest and blood came out even when I was sneezing.

But to sum it up, I was so fearful when I got the news that I've tested positive. But the whole treatment experience with the drips was a God-send, unexplainable. The doctor took care of me very well. He phoned me every day to check up on me. After 5 weeks I've started working normally, lifting heavy things with all the others. During the first 3 weeks I've lost a lot of weight, but the 2 weeks after that I've picked up the weight that I've lost. I don't feel any pain in my body anymore, not an inch.

I'm also a diabetic. After I've recovered from Covid, I'm doing much better in this regard as well. My sugar levels before treatment was between 16 and 17 and sometimes even up to 20. The highest since my treatment was 10. My levels range between 10 and 7.5. Even now I feel so much better and can do anything I want. I don't feel like I am diabetic anymore. I am still using the NAD+Phyto every day.

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Disclosures

Dr AF van Wyk and Theo Verwey are the founders of NAD+ OSCILLATION THERAPY (NOT). NAD+Phyto was developed by Theo Verwey. The NAD+/NADH Analyzer (based on

the NAD calculator) is the combined work of Theo Verwey and Dr Adriaan Francois Van Wyk. The NAD calculator is the sole work of Theo Verwey.

Figures

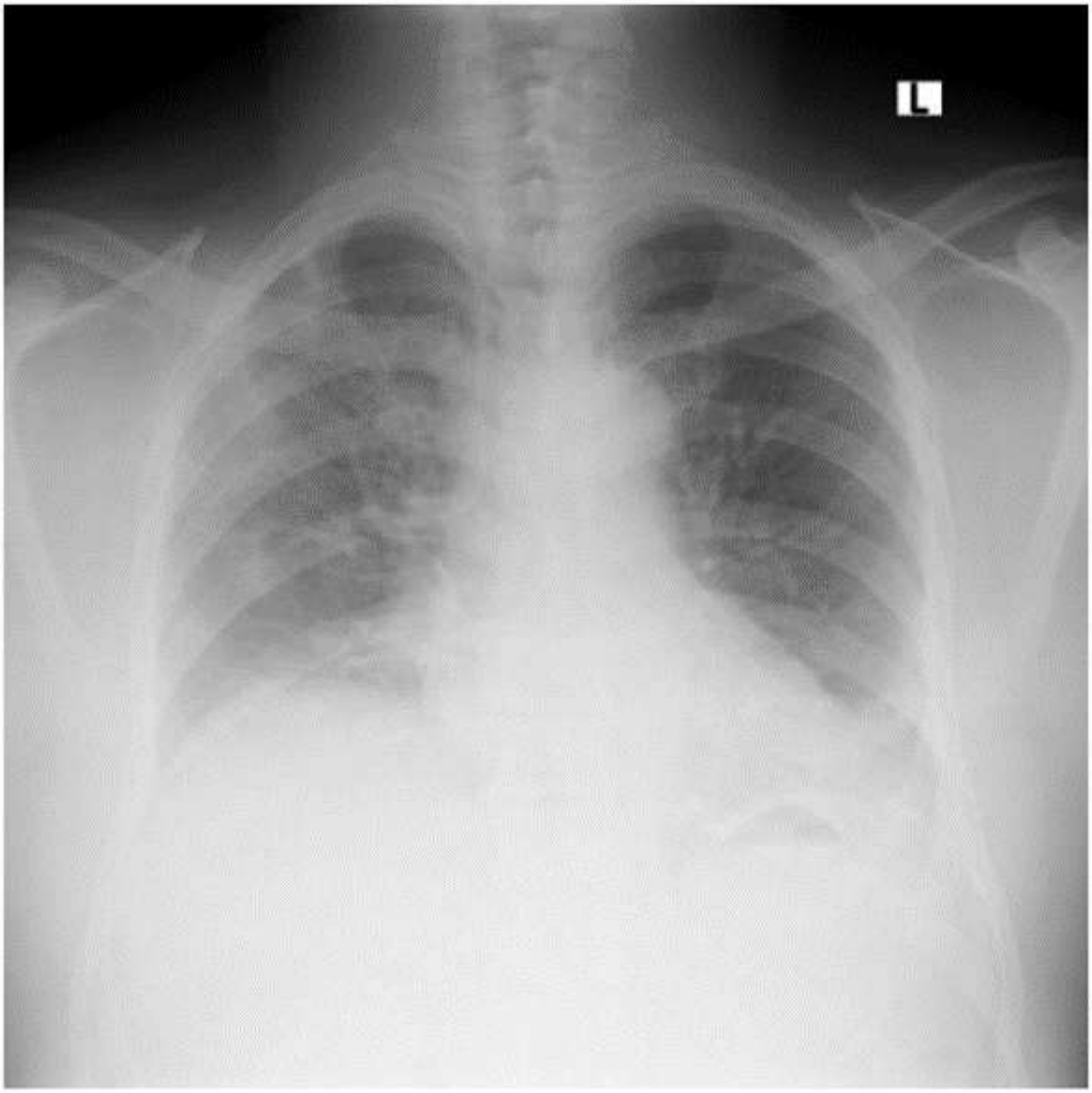


Figure 1

Chest X-Rays Report (23 June 2020): Bilateral patchy and striated groundglass opacity more prominent right lung and left lower lobe. Bilateral lower lobe atelectasis.

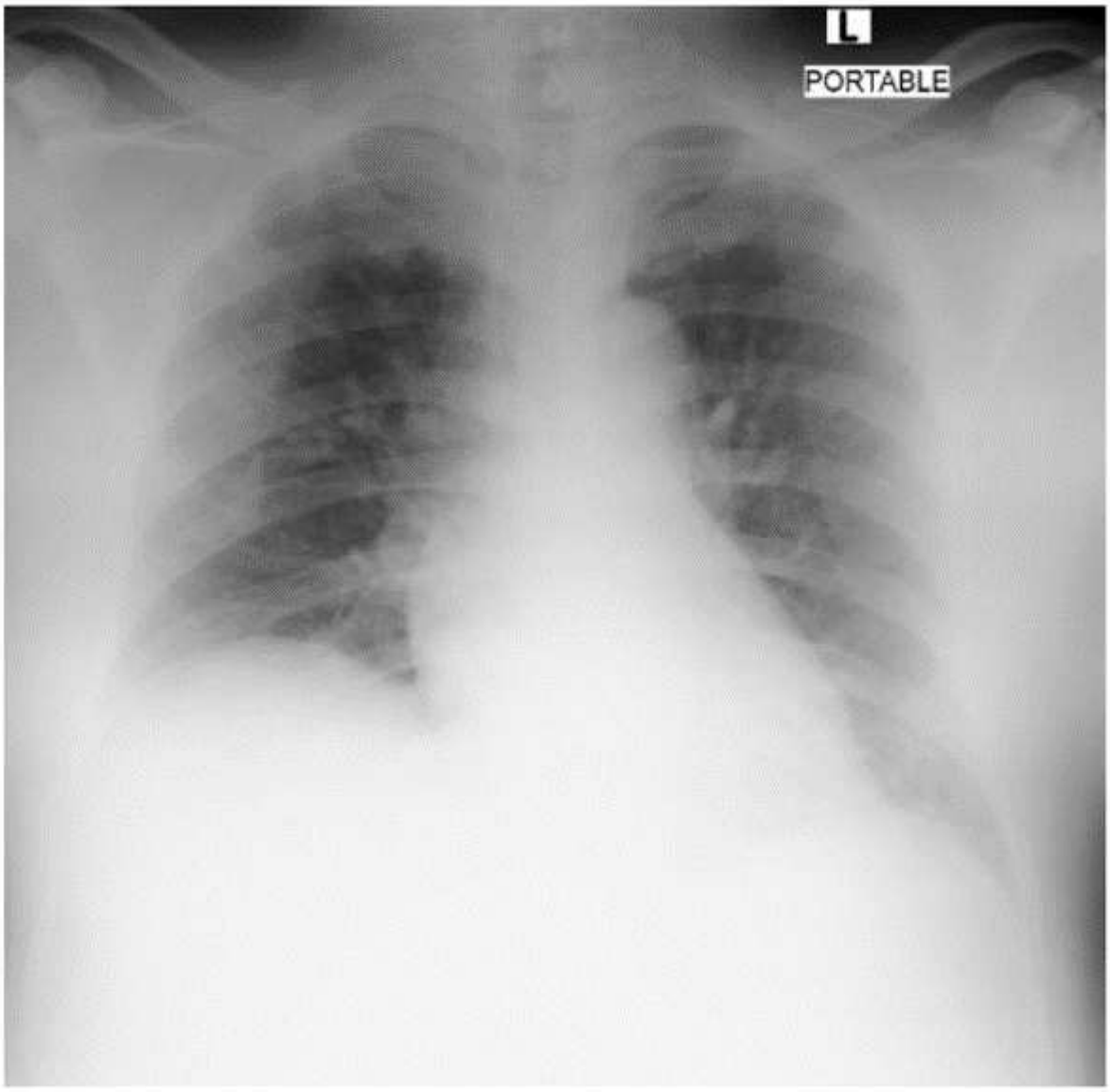


Figure 2

Chest X-Rays Report (26 June 2020): Perihilar bronchial cuffing and tram tracking is suggestive of bronchitis. No discrete consolidation or groundglass opacity to suggest a fulminant Lower respiratory tract infection or COVID-19.

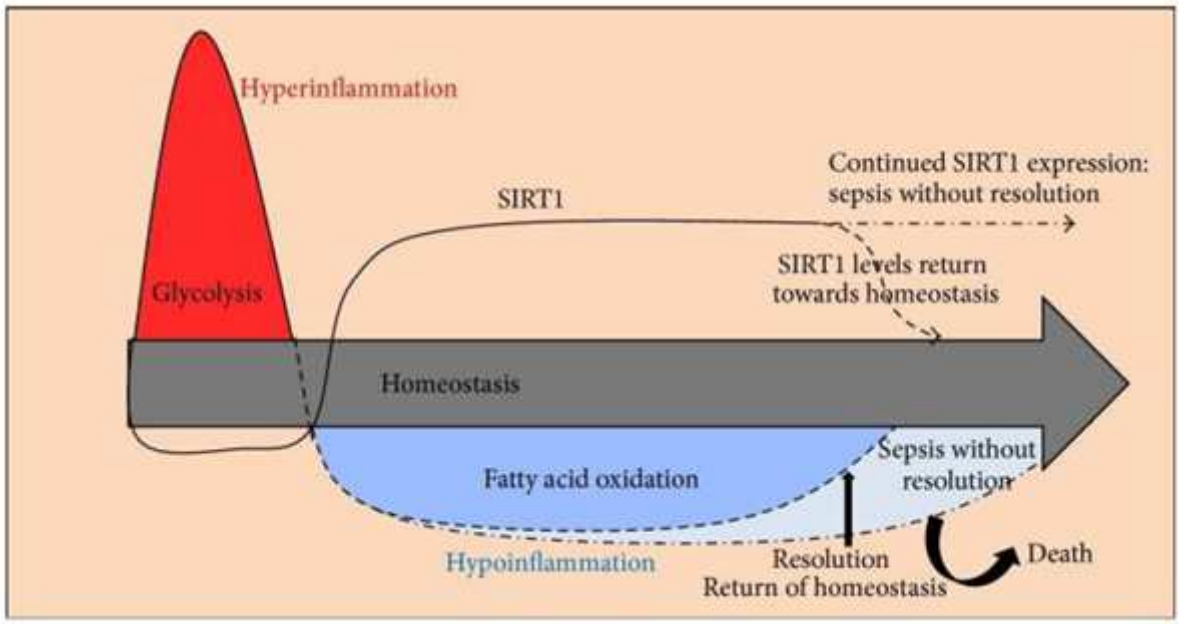


Figure 3

Sirtuins and acute inflammation of sepsis: the extreme stress response of sepsis rapidly induces a systemic and potentially lethal hyperinflammatory state (red), which shifts within hours to a counterreactive hypoinflammation/adaptation phase (blue). NAD+ activation of sirtuins directs this switch. Mechanistically, nuclear SIRT1 levels briefly drop when homeostasis deviation initiates the glycolysis-dependent hyperinflammation, but within hours nuclear and mitochondrial sirtuin activation shifts glycolysis to fatty acid oxidation. This metabolic reprogramming globally represses immunity, affecting neutrophils, monocytes, dendritic cells, NK cells, and T lymphocytes. Resolution of acute inflammation and sepsis rebalances sirtuins and inflammation to restore homeostasis. Persistent elevation of sirtuins and hypoinflammation as a result lead to death (denoted by light blue area).(2)

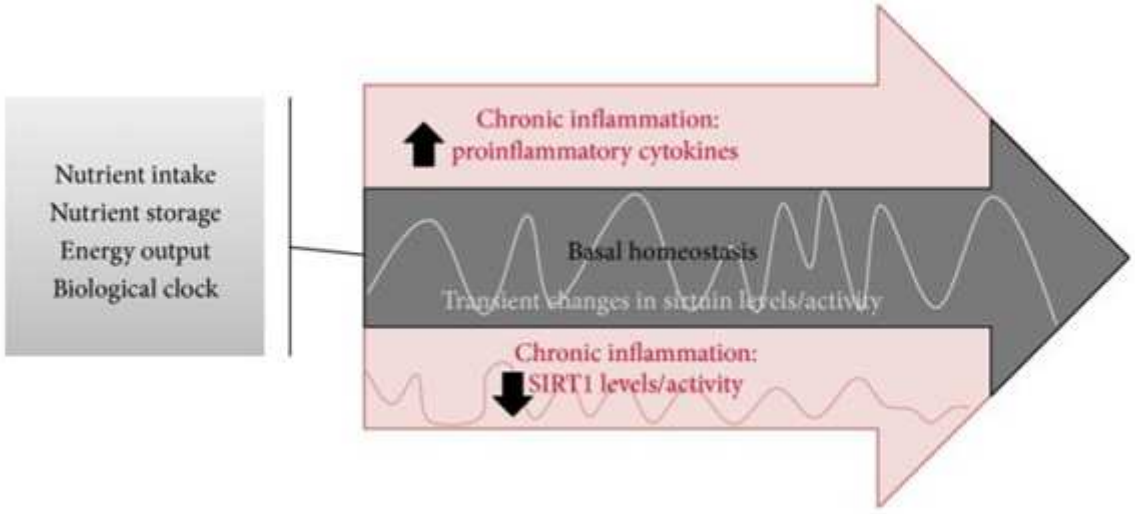


Figure 4

Sirtuins and chronic inflammation: during homeostasis (grey arrow), there are small perturbations in sirtuin levels without inflammation. During chronic inflammatory states (denoted by pink), persistent decreases in SIRT1 levels/activity sustain glycolysis-dependent proinflammatory pathways. This immunometabolic inflexibility alters the bioenergy homeostasis set point, which is rebalanced by increasing SIRT1 activity (2)

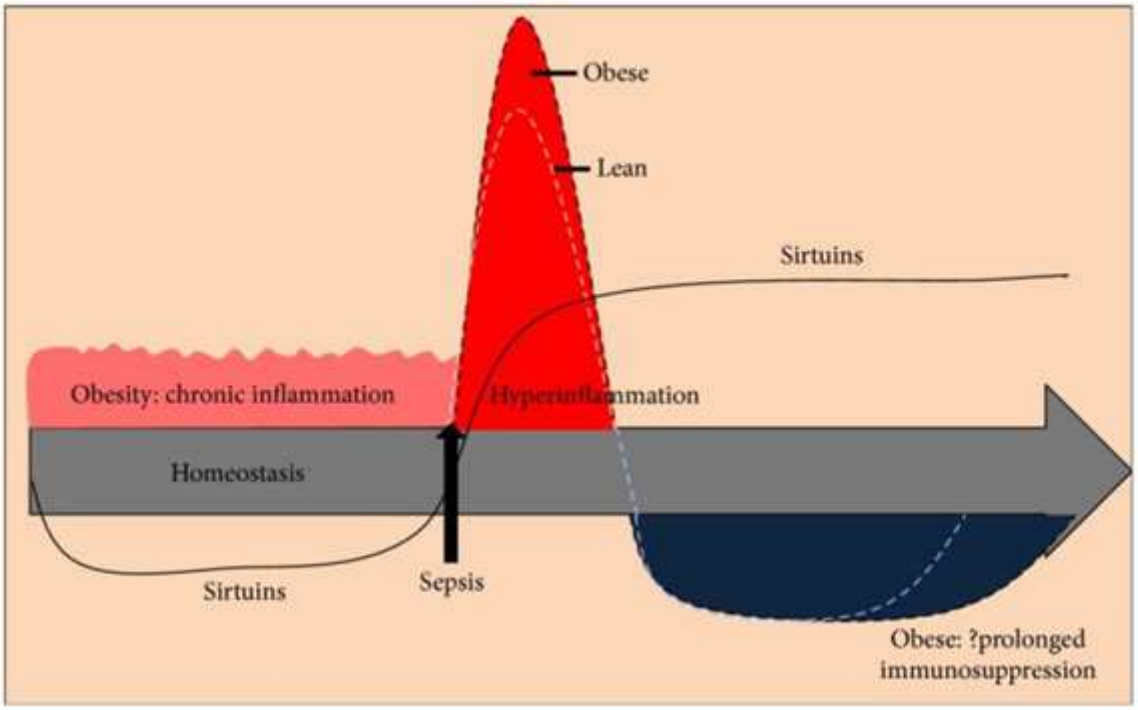
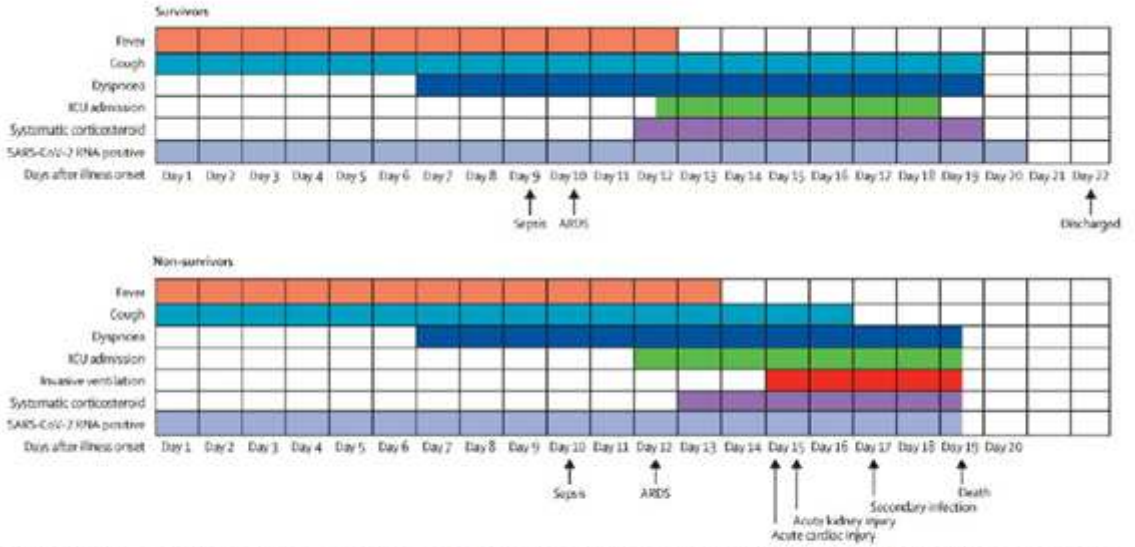


Figure 5

Sirtuins and obesity with sepsis: obesity is associated with low-sirtuin levels/activity, but mechanisms responsible for this imbalance are unknown. If sepsis occurs in obese individuals with low SIRT1, the early hyperinflammatory phase is accentuated and counteractive adaptation stage may be prolonged. Activating SIRT1 before obesity-associated sepsis prevents the accentuated acute inflammatory reaction. (2)



Clinical courses of major symptoms and outcomes and duration of viral shedding from illness onset in patients hospitalised with COVID-19 - Figure shows median duration of symptoms and onset of complications and outcomes. ICU=intensive care unit. SARS-CoV-2=severe acute respiratory syndrome coronavirus 2. ARDS=acute respiratory distress syndrome. COVID-19=coronavirus disease 2019.(14)

Figure 6

Clinical courses of major symptoms and outcomes and duration of viral shedding from illness onset in patients hospitalised with COVID-19 -

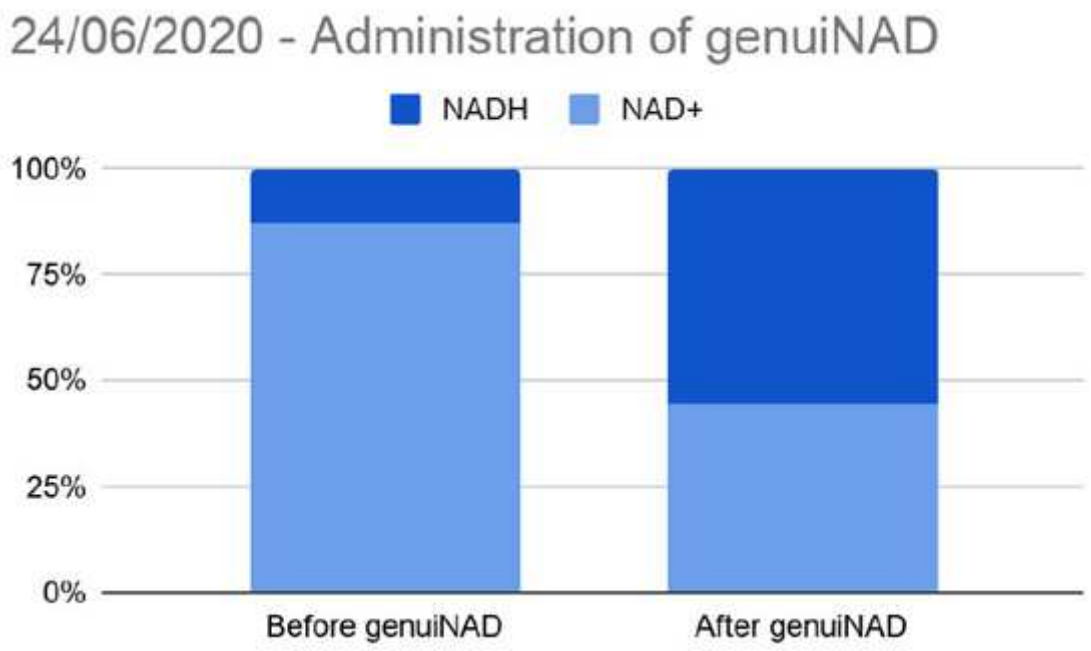


Figure 7

Graph 1 - NAD+/NADH ratio before and after genuiNAD. The aim is to modulate the adaptation phase of the immune response by normalizing the NAD+/NADH ratio to 50/50. NAD+/NADH Before = 87/13 After 44/56

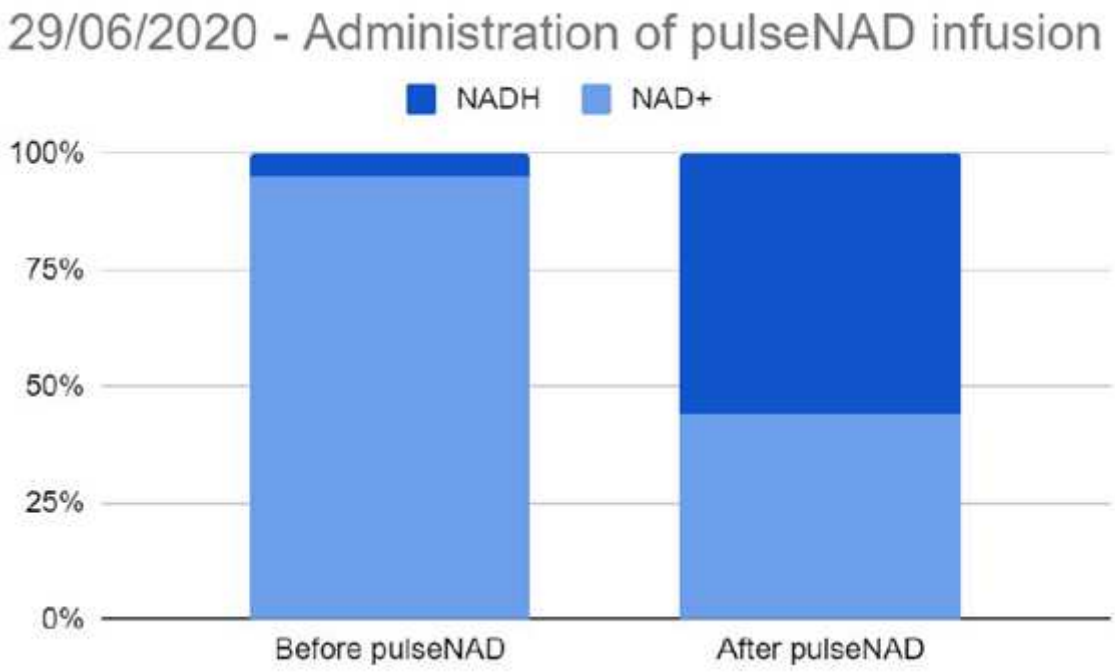


Figure 8

Graph 2 - NAD+/NADH ratio before and after pulseNAD. The aim is to modulate the adaptation phase of the immune response by normalizing the NAD+/NADH ratio to 50/50. NAD+/NADH Before = 87/13 After 44/56

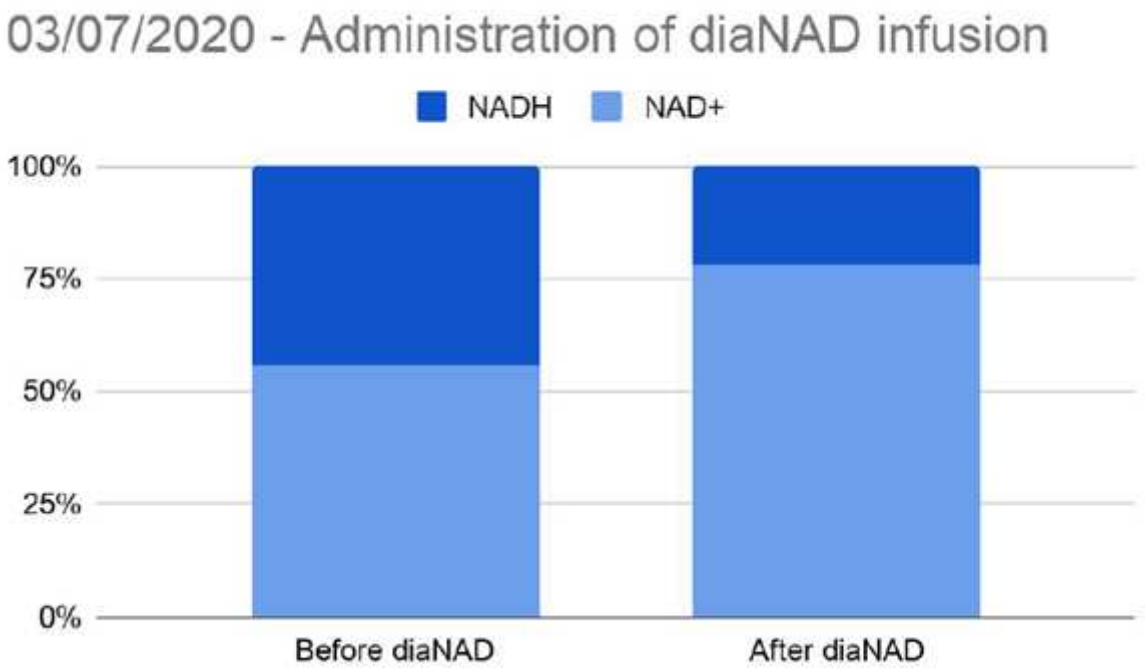


Figure 9

Graph 3 - NAD+/NADH ratio before and after diaNAD. The aim is to modulate NAD+/NADH ratio to improve the management of Diabetes Mellitus Type 2. NAD+/NADH Before = 56/44 After 78/22.

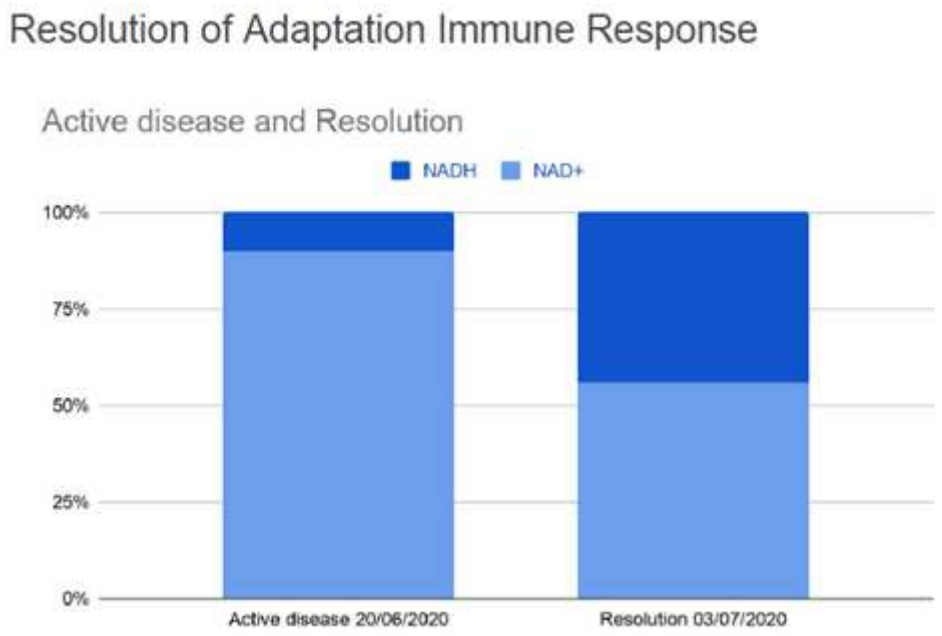


Figure 10

Graph 4 - Resolution of the adaptation / hypoinflammatory phase of the immune response. NAD+/NADH ratio indicates return to homeostasis.

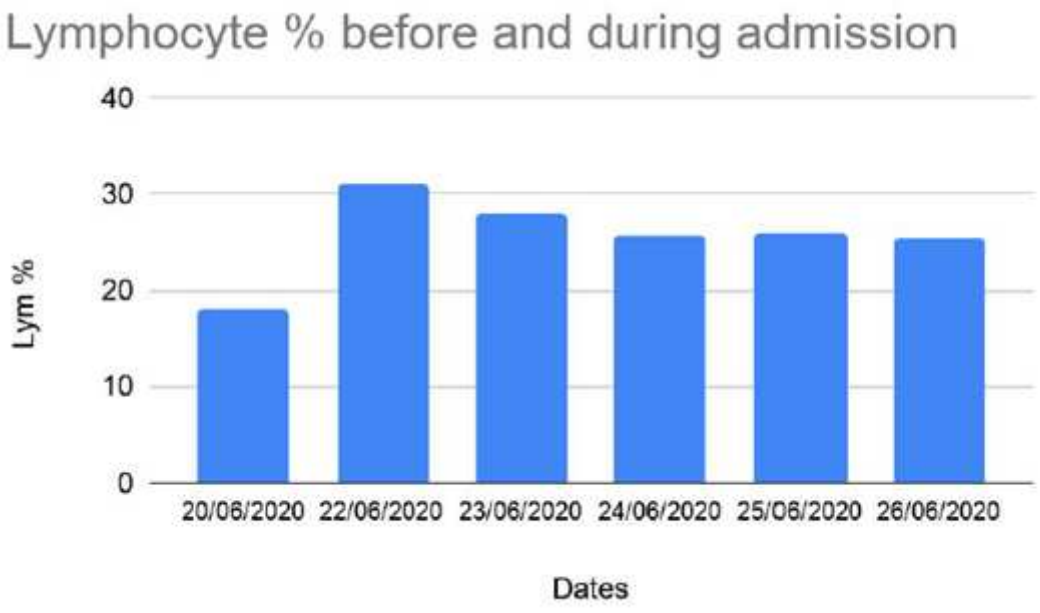


Figure 11

Graph 5 - Lymphocyte % before and during admission

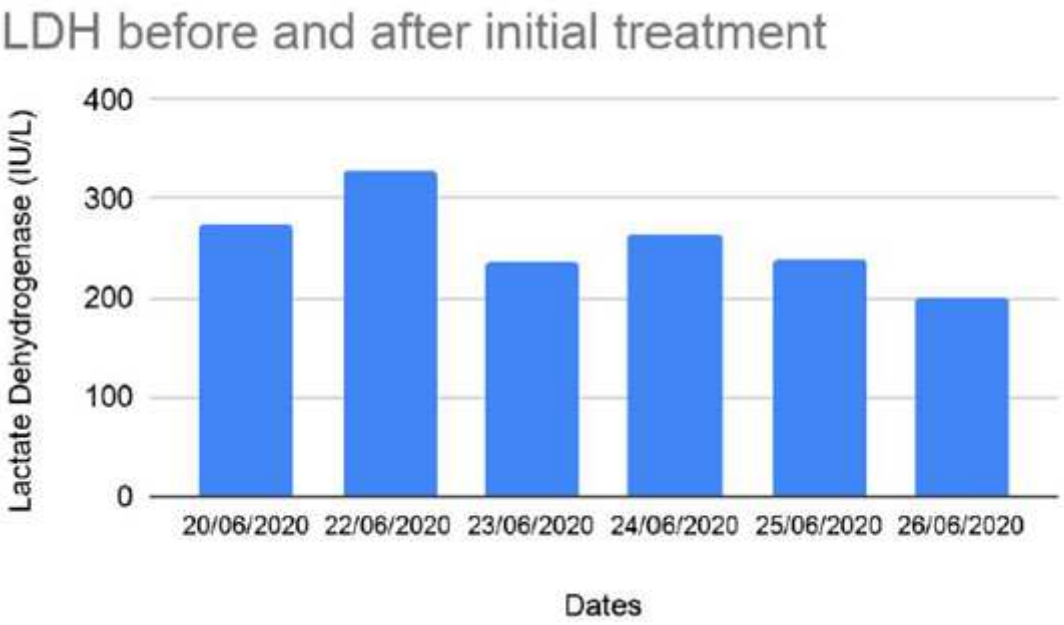


Figure 12

Graph 6 - Normalisation of LDH levels.

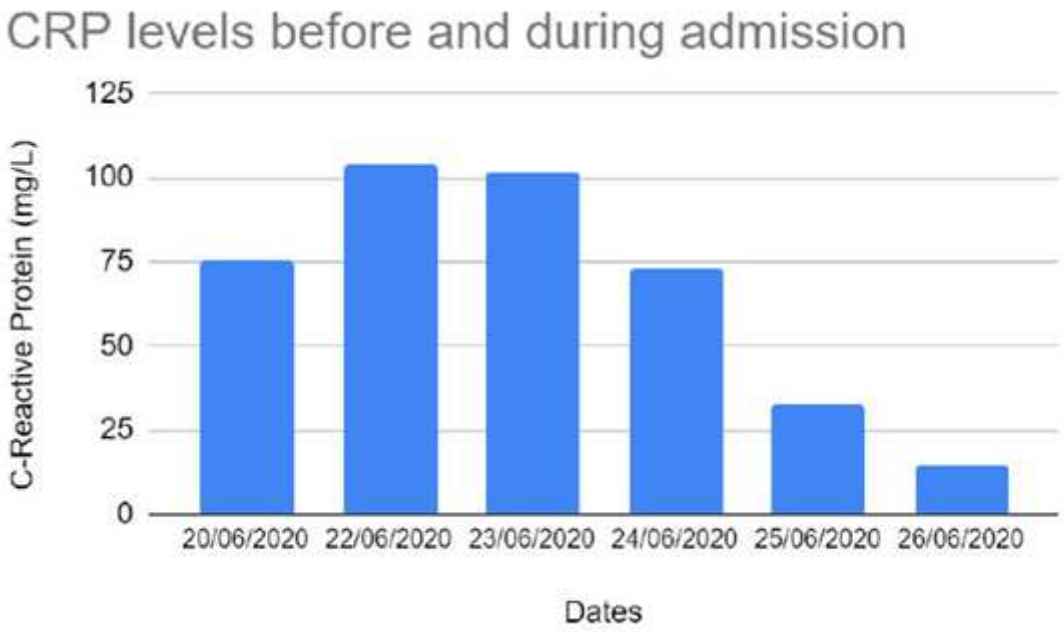


Figure 13

Graph 7 - C-Reactive Protein levels decreased indicating decreased inflammation.