

Pseudoexfoliation Syndrome Post COVID vaccination

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Abstract

In an attempt to rapidly control of the unprecedented effects of the COVID-19 pandemic, a series of vaccination programmes were rapidly rolled out across the world, with a paucity of studies on their side-effects or efficacy. Lack of testing may be the reason for why there have been an increasing number of reports of new-onset autoimmune phenomena following COVID-19 vaccination. These conditions include immune thrombotic thrombocytopenia, autoimmune liver diseases, Guillain-Barré syndrome, IgA nephropathy, rheumatoid arthritis and systemic lupus erythematosus). It has been postulated that production of autoantibodies may have been due the use of certain vaccine adjuvants such as PEG, used by Pfizer (Chen et al, 2022). These side-effects are somewhat more serious than the systemic side effects seen following 2 injections of the Oxford-AstraZeneca (ChAdOx1 nCoV-19) COVID-19 vaccine (58.75%), or BNT162b2 (68.5%) (Menni et al, 2021). Metabolic testing of a 71 year old man, of excellent health with no predisposing sequelae apart from his age was performed following triple vaccination against COVID. Organic Acids Testing (OAT) of urine was used to determine the metabolic abnormalities following COVID vaccination at 4, 8 and 12 weeks post vaccination. Subsequent to this time the patient complained of vision loss and upon visiting an ophthalmologist was diagnosed with Pseudoexfoliation syndrome. Examination of the OAT data revealed significant increases in markers associated with vitamin B2 and vitamin B12 deficiency. The markers were consistent with an extensive and prolonged inflammatory response to a combination of 2 injections of ChAdOx1 nCoV-19, followed by 1 injection of BNT162b2. The inflammatory response, included markers of extensive oxidative stress, which has subsequently lead to the development of irreversible eye damage typical of Pseudoexfoliation syndrome in an otherwise perfectly healthy individual.

Keywords: COVID vaccine, Long Vax, Pseudoexfoliation Syndrome,

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Introduction

The outbreak of the Covid-19 pandemic in late 2019 lead to the rapid development of several vaccines designed to immunize against Covid-19 infection. Two of these vaccines were based on mRNA technology (Pfizer/BioNTech (BNT162b2, brand name Comirnaty) and of Moderna (mRNA-1273, brand name COVID-19 Vaccine Moderna). The principle behind the mRNA vaccine was rather simple in that the mRNA in the vaccine would be taken up by cells (of an unspecified type), whereupon the mRNA would be “read” and viral proteins expressed on the surface of the unspecified cell, and thereby stimulate the

immune response. As part of the formulation, the mRNA was encapsulated within a lipid nanoparticle, which for some unknown reason (or none that we could find) was coated with poly-ethylene-glycol (PEG). What is curious about this choice is that PEG was originally designed as a mechanism to “avoid” the immune response, which is contrary to the normal purpose of a vaccine, to stimulate the immune response.

Part of the vaccine strategy was the absolute requirement of persons, particularly those over 50 to be injected with the vaccines, as they were excluded from places of entertainment, bar, clubs, and even shopping centres, and had to show proof of vaccination. The vaccine was “sold” to the public as being safe, yet soon it became apparent that many people experienced significant side-effects from the vaccine, such as a bad headache or bellyache that doesn’t go away for a long time, even with pain medication, blurred vision, difficulty with speech, drowsiness, seizures, shortness of breath, chest pain, and swelling in your leg. Over time, it became apparent that the vaccines could elicit symptoms similar to those of prolonged COVID infection (Long COVID), and a condition of “Long Vax” could result (Couzin-Frankel and Vogel 2022). In which there was a higher incidence and severity of neuropathic symptoms and dystonia. In addition, both Long COVID and Long Vax can result in symptoms similar to chronic fatigue syndrome, and may also include clinical symptoms affecting the respiratory system, neurological/psychiatric, the musculoskeletal system, cardiovascular, autonomic, gastrointestinal system and the mucus membranes (Koutsiaris et al, 2022). Hence in many cases the vaccine is FAR from safe.

We report the alterations in the metabolism of a 71 year old man who received both the Astra-Zeneca and Pfizer-BioNTech vaccines, resulting in significant metabolic deficiencies, which lead ultimately to the development of sight-threatening Pseudoexfoliation Syndrome (PEX).

Methods

The Oxford-AstraZeneca (ChAdOx1 nCoV-19) COVID-19 vaccine was given as two doses administered 2 months apart, followed 3 months later by the Pfizer-BioNTech (BNT162b2) vaccine. Vaccinations on 10/06/21, 16/08/21, 14/01/22, OAT 14/07/22, 19/08/22, 7/02/23; PEX detection on 31/07/23. An Organic Acids Test (Oasis Laboratories) was used to monitor various biochemical parameters of the subject before vaccination and for 4 intervening times post the vaccination. Intraocular pressure was measured with a Goldmann Applanation tonometer, and Visual Field Testing performed. Diagnosis of Pseudoexfoliation syndrome (PEX) occurred on 31/07/23 with approximately 20% field loss in Left eye, with intraocular pressure was R39, L46. Xalatan™ and Cosopt™ drops were prescribed and retesting was performed one month later (R15, L20), at which time Alphagan™ was prescribed. Two months later, IOP had reduced to R12, L14, however visual field loss had reached over 40% in the left eye.

Results

Alterations in metabolism were found using OAT data recovered before and during recovery from COVID-19 vaccination (Figures 1, 2, 3 and 4). The following deficiencies were found:

Pseudoexfoliation Syndrome Post COVID Vaccination

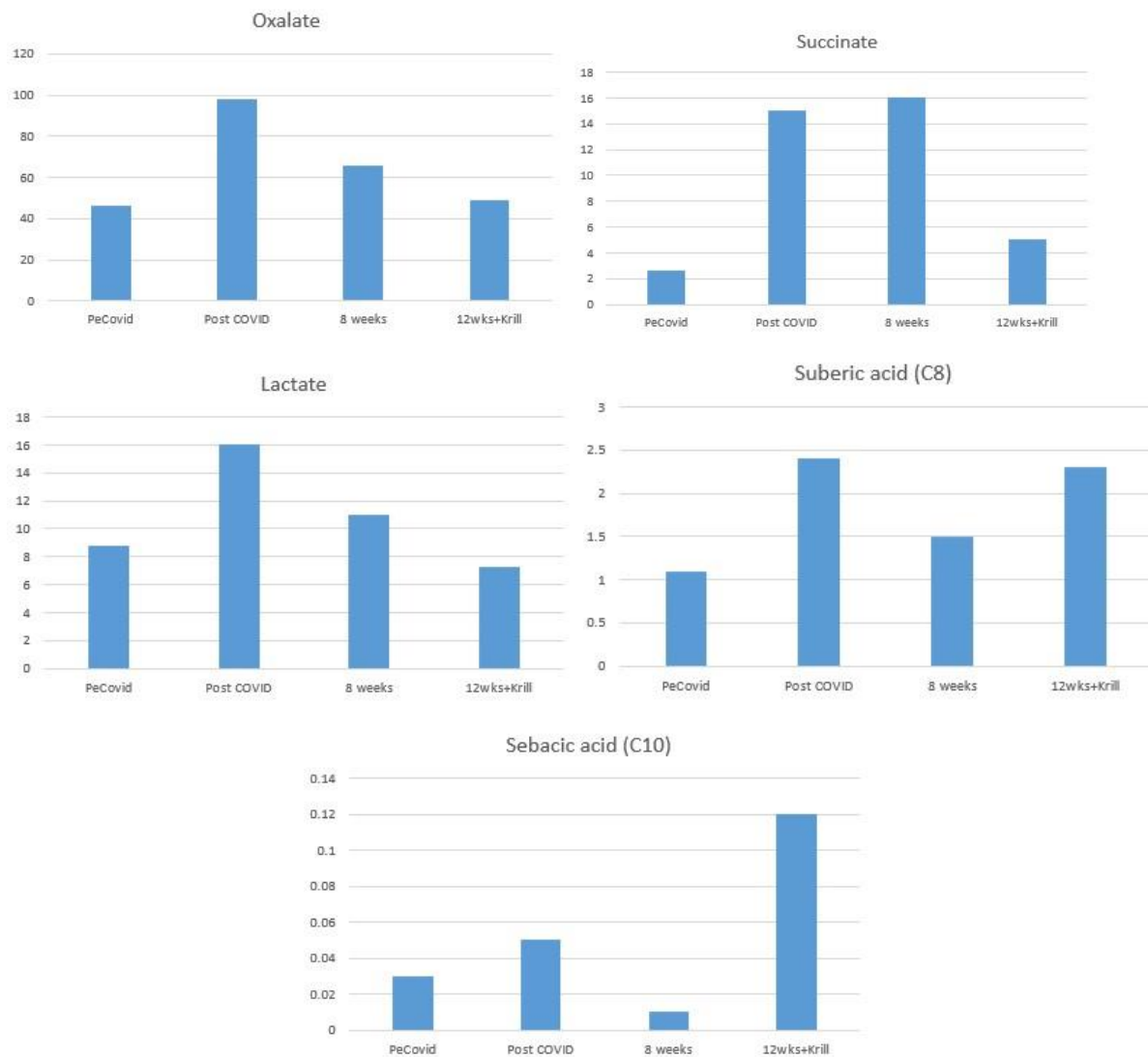
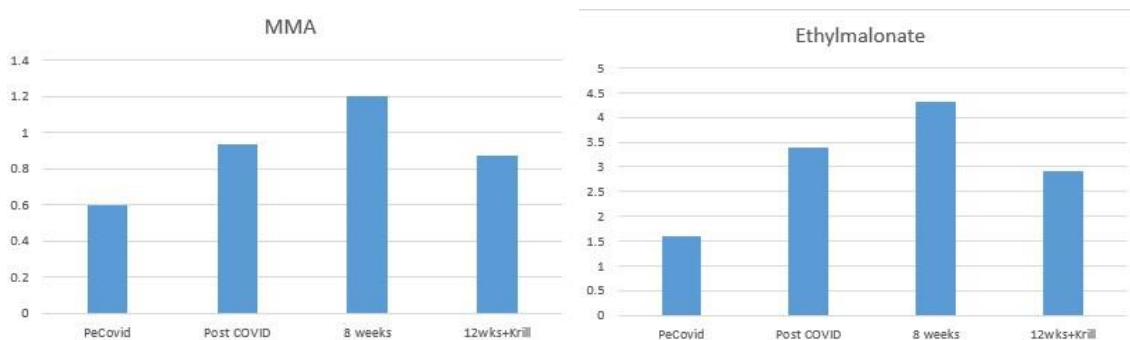


Figure 1. Urinary Organic Acids Indicative of functional vitamin B2 deficiency. Markers included oxalate, succinate, and lactate and the fatty acid markers, suberic acid, and sebatic acid.



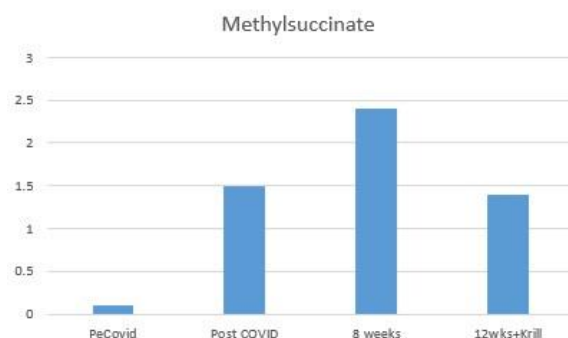


Figure 2. Urinary Organic Acids Indicative of Adenosyl vitamin B12 deficiency, including MMA (Methylmalonic acid), Ethyl malonic acid and methyl succinate.

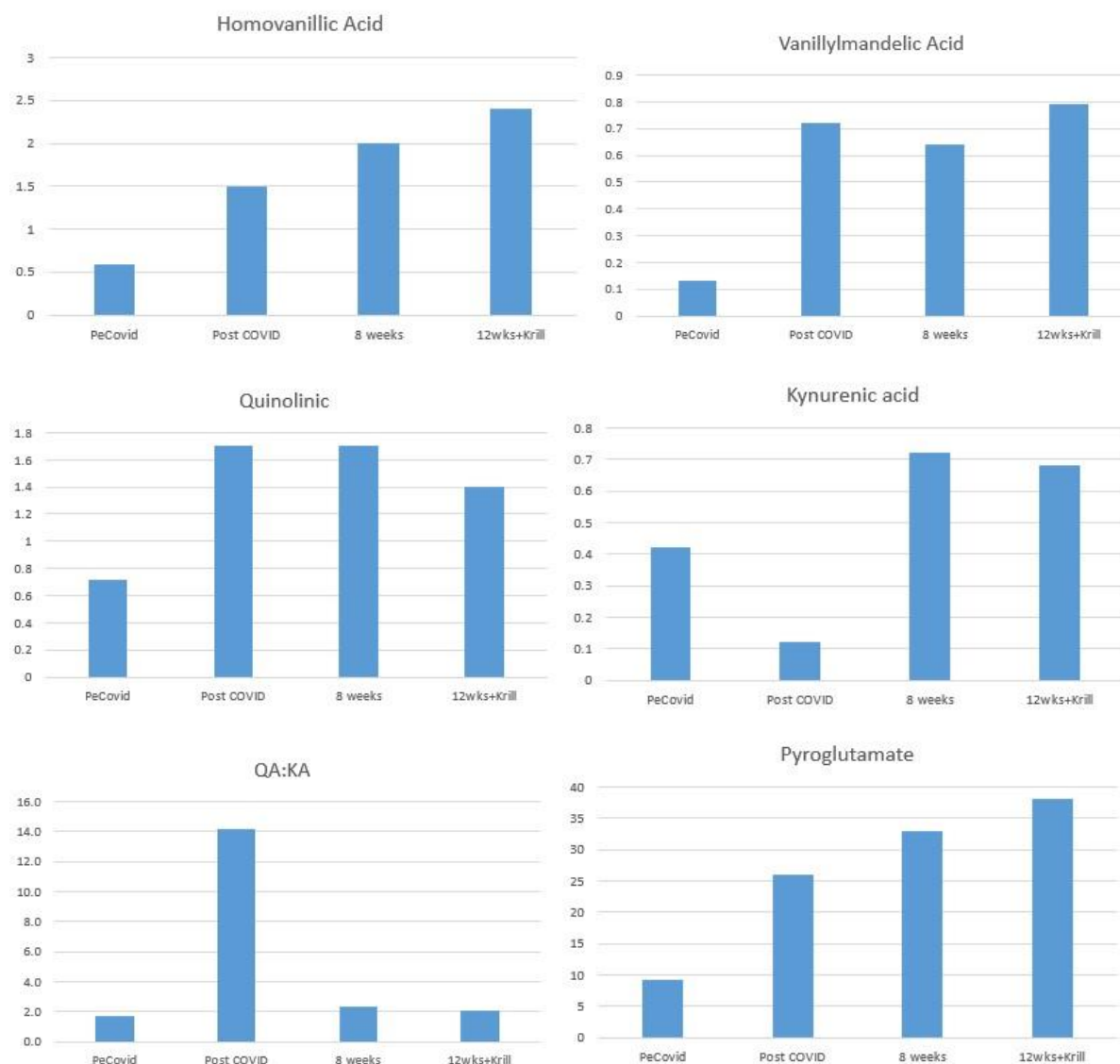


Figure 3. Urinary Organic Acid markers Indicative of Methyl vitamin 12 deficiency, including Homovanillic acid, Vanillyl mandelic acid, Quinolinic Acid (QA), Kynurenic Acid (KA), and the QA:KA ratio (indicative of Iodide/Selenite deficiency) and Pyroglutamic acid.

Markers of functional B2 deficiency (Figure 1) and functional Adenosyl B12 deficiency (Figure 2), as well as functional Methyl B12 deficiency (Figure 3) were all elevated, 4, 8 and 12 weeks post COVID vaccination with Pfizer-BioNTech (BNT162b2) vaccine. Elevated Pyroglutamic acid (Figure 3) is

indicative of lower glutathione synthesis, and is a feature of functional B12 deficiency, and has been correlated with oxidative stress in a wide range of conditions, including PCOS (Turatham et al, 2022), Septic shock (Gamarra et al, 2019), Sepsis (Gueta et al, 2020); acute kidney injury (Davidson et al, 2022), and pulmonary viral infections (Oiry et al, 1999).

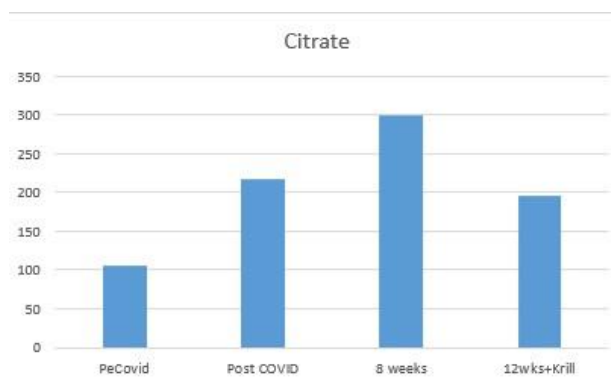
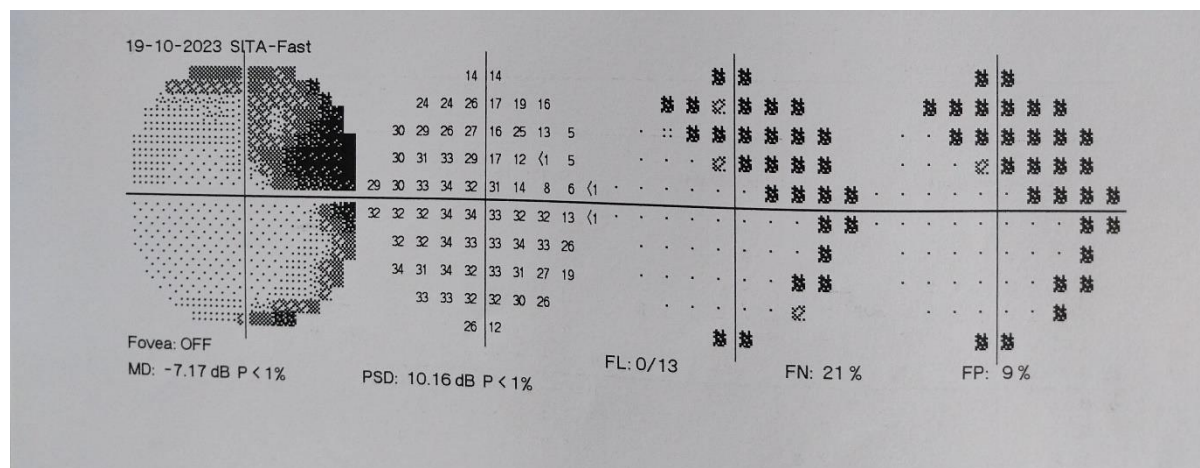


Figure 4. Urinary Organic Acid markers Indicative of functional iron deficiency

Evidence of excessive use of iron could be seen by the uncoupling of the iron-sulphur protein enzyme aconitase, resulting in elevated citrate (Figure 4).

OAT analysis revealed a dramatic increase in markers associated with functional vitamin B2 deficiency, including oxalate, succinate, lactate, and suberate from 4 weeks post vaccination, extending until at least 3 months post vaccination. The deficiency was accompanied by increases in the methyl B12 deficiency markers, HVA, VMA, QA, KA and pyroglutamate and the Adenosyl B12 deficiency marker MMA. There was no resolution in the B12 deficiency markers 3 months after the COVID vaccination.

The subject complained of visual loss at night, which would resolve with the use of non-steroidal anti-inflammatories. It was this loss that induced the subject to seek the help of a local ophthalmologist. At the time of first assessment, it was 18 months after the last injection with the Pfizer vaccine Visual Field Optical scanning revealed rapidly progressing loss of vision in the left eye of the subject. In the first scan, visual loss was around 20% with IOP 44L, 41R eye (Figure 5 upper panel). Little loss of vision in the right eye (not shown) Four weeks later, following treatment with Xalatan and Cosopt, IOP had reduced to 24L/19R and eight weeks post start of treatment visual loss had increased to over 50% with IOP 14L, 12R eye (Figure 5 lower panel).



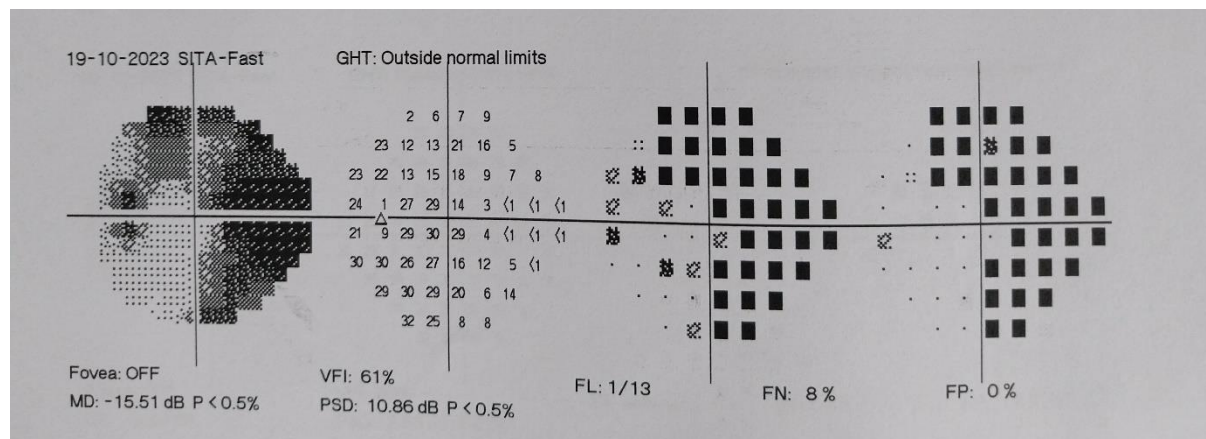


Figure 5. Visual Field Optical scanning of the left eye of the subject. Upper panel scanning on the first visit to an ophthalmologist, lower panel, scanning one month later. Black dots represent areas of the eye non-responsive to light.

Discussion

Evidence suggests that the pressure change seen in the eye is due to some sort of progressive response, and there is mounting evidence to suggest that there is a strong role of the immune response in the development of glaucoma (Kamat et al, 2016) with several workers suggesting some sort of autoimmune response as being causative for the condition (Rieck 2013; Gru et al, 2008; Bakalash et al, 2002; Tezel and Wax 2004). Prolonged immune responses, such as those seen with COVID infections or COVID vaccination, have been shown to result in significant oxidative stress, with reduction in levels of active vitamin B12, and an accompanying increase in levels of homocysteine. In many cases the response to vaccination is similar to that seen in Long Covid, and has been termed Long Vax. In this regard, elevated homocysteine levels are a feature of PEX (Koc and Kaya, 2020; Rebecca et al, 2019), and so would be associated with functional B12 deficiency (as per data). There are many reports of COVID-19 vaccine associated ocular adverse effects (Ichhpujani, et al, 2022a; Habot-Wilner et al, 2023; Pang et al, 2022; Singh et al, 2023; Mahandrades et al, 2023; Chaudry et al, 2023; Pillar et al, 2023; Wang et al, 2022; Kamo, and Ohno-Matsui 2024, Guo et al, 2023) as well as various ocular manifestations of COVID-19 (Ichhpujani, et al, 2022b; Ashkenazy et al, 2022). Apart from the above there are an increasing number of rarer conditions occurring, such as VHL syndrome, and some common complications such as cerebrovascular disorders, including transient ischemic stroke, venous sinus thrombosis, intracerebral haemorrhage, and demyelinating disorders including MS, neuromyelitis optica, and transverse myelitis (Hosseini and Askari, 2023), and various other neurological conditions (Chatterjee and Chakravarty, 2023). In addition, there has been an increase in multi-system Inflammatory Syndrome (Elsaid et al, 2023), and many neurological complications after the first dose of vaccine and subsequent COVID (Patone et al, 2021). These complications have been documented since 2021, with increasing reports of problems from 2022 onwards, and yet governments have not moderated their calls for vaccination, and as such should be liable for the damage from the vaccines.

The prolonged response as described above, as well as all of the Long Vax-type reports could potentially be caused by the abnormal biodistribution due to PEGylation of the mRNA-lipid nanoparticles. PEG-nanoparticles have been shown to shield the nanoparticles from opsonization and phagocytosis, thereby prolonging circulation time, and completely

changing the biodistribution from that observed with non-PEGylated nanoparticles, as such are ideal for protein delivery. In contrast, however, they are NOT what is required to stimulate a prolonged immune response, which is targeting to the local lymph node and liver, which is what is required from vaccination. In contrast PEG-nanoparticles are much more likely to promote numerous systemic complications, such as those described above (Suk et al, 2016).

The control of the inflammatory process is intimately dependent upon Selenium and its role in the activation of glutathione peroxidase. Part of the inflammatory cascade involves the activation of oxygen by NADPH Oxidase to generate the reactive oxygen species O_2^{**} ; This in turn is further activated to generate hydrogen peroxide (H_2O_2). Under normal circumstances the H_2O_2 is then converted to hydroxide and then water by the Selenoprotein Glutathione-Peroxidase (GSHPx(Se)). In Selenium deficiency this reaction is reduced and so dangerous H_2O_2 can accumulate inside the cell and cause massive intracellular damage. Control of oxidative stress involves the anti-oxidant molecule GSH, and the reduction of oxidized glutathione (GSSG) requires the FAD-dependent enzyme glutathione reductase (GSH reductase). In Selenium deficiency activation of vitamin B2 is incomplete and hence levels of FMN and FAD are lower inside the cell. This has the dual effect of reducing the activity of GSH-reductase, but also, because of the requirement for FMN and FAD in the cycling of methyl B12, lack of FMN and FAD also leads to lower methylation and reduced production of GSH, through lower activity of the sulphation cycle in Methyl B12 deficiency. The result would be a greatly increased reaction of H_2O_2 and potentially cause death due to an over-active inflammatory response. Oxidative stress is further increased because methyl B12 is required for the production of the cellular anti-oxidant, melatonin. The prolonged immune response generated by the combined Astra Zeneca viral vaccine, coupled with boosting via the Pfizer BioNTech which is further exacerbated by the PEGylation of the mRNA-nanoparticle vaccine, appears to have resulted in a prolonged Inflammatory response, and would be expected to result in reduced levels of Selenium in the aqueous humour, thereby exacerbating the inflammatory response in the eye, with resultant increased damage to the optic nerve. In this regard, reduced Selenium levels are common in the aqueous humour in PEX (Yilmaz et al, 2011).

Examination of the OAT data with time supports the above hypothesis. Hence, at 4 weeks post Covid vaccination there is an increase in the functional B2 deficiency markers, succinate, lactate, oxalate, suberate and the FMN deficiency marker the QA:KA ratio. With further time, evidence of the secondary effect of functional B2 deficiency can be seen in the increase in the functional B12 deficiency markers, QA, KA, HVA, VMA, Pyroglutamate, MMA, ethylmalonate, and methylsuccinate. Potentially the resultant lack of methylation would have deleterious effects on the methylation of lysine and of various proteins, leading to structural alterations, which in turn could lead to autoimmunity reactions, and formation of protein aggregates, typical of PEX.

Conclusions

The compulsory vaccination of the subject with the COVID vaccine, has resulted in a deleterious reduction in functional vitamin B2 and vitamin B12 levels, leading to an increase in oxidative stress markers, elevation in blood pressure, and ultimately has contributed to the induction of elevated intraocular pressure, and Pseudoexfoliation syndrome and the potential loss of sight in an otherwise extremely healthy individual. Apart from the devastating loss of sight, this has been accompanied by repeated bouts of depression in an individual who was previously known to be a highly optimistic person with an "Up-beat" personality. The lack of understanding of the biochemistry of this response and the lack of responsibility shown by the medical profession and the local health department and the Therapeutic Good Association has been outstanding. A vaccine that ultimately threatens the

sight of the vaccinated, should never have been released onto the market, nor made mandatory for the general public.

Declarations

Ethics approval and consent to participate – Not Applicable

Consent for publication – Not Applicable

Availability of data and material – All data is included in the manuscript

Competing interests – the author declares no competing interest

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Dr Gregory Russell-Jones was the sole contributor to the manuscript

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