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OIRF publications.

*An exclusive translated **article for Praxis2Practice Supporters**,  
published February 2023 by Praxis2Practice Consulting . . .*

## Ozone Therapy for the Treatment of Post-Covid Syndrome

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**From an article in *Erfahrungsheilkunde*, Volume 71, Issue #5, 2022  
Machine Translation by Lernout & Hauspie, LogoMedia & Promt  
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### Abstract

Post-covid Syndrome is a complex disease, but it can be successfully treated by an integrated treatment approach with a combined application of individual orthomolecular substances. A clarification of the background symptoms and the need for integrative treatment at the earliest possible time is important. In the case of Epstein-Barr virus, similar courses are known without leading to corresponding media fear-mongering representations. Within the framework of a multimodal treatment approach supported by individual laboratory diagnostics, ozone therapy is an important basic measure. The tolerability is very good and shows modulatory effects on immunological factors in the sense of regulatory medicine. Furthermore, antioxidant capacities are improved.

**Keywords:** Ozone therapy, Post-Covid syndrome, Long-Covid, Corona pandemic, Covid-19, Fatigue

Not the least because of the Corona pandemic, secondary phenomena after viral diseases have come much more into focus than was the case 2 years ago. Post-Covid syndrome impressively shows that in some instances after a viral illness massive symptoms can also occur in the long term. Particularly in the foreground are fatigue and exhaustion conditions. These are also known as the result of an Epstein-Barr virus infection (EBV) only so far they are not really recognized and rather are considered a psychological “problem”. Now hopefully through the knowledge from the Corona pandemic a broader understanding occurs so that these patients are also taken seriously and the symptoms are considered as organically caused.

## **Definitions**

### **Fatigue**

In the area of post-viral secondary problems fatigue syndrome is very central. There are certain definitions to keep in mind here:

- Fatigue = Symptom: a physical, mental and/or emotional kind of exhaustion disproportionate to the previous efforts which cannot be eliminated by sleep and thus are pathological
- Post-viral Fatigue = emerges after viral illness
- Fatigue plus = Added to fatigue there are other symptoms such as muscle pain, neurocognitive symptoms such as concentration disturbances and exercise intolerance
- ME/CFS = Complex, acquired illness of neuroimmunological genesis (G93.3)
- Chronic fatigue = fatigue in the context of a chronic disease that determines the ICD-10 coding, e.g. in the context of multiple sclerosis

### **Long-Covid or Post-Covid Syndrome**

According to estimates from WHO about 10% of Covid-19 patients still suffer from persistent symptoms 12 weeks after infection, even if they did not need treatment in the clinic<sup>(1)</sup>. Accordingly infection with the multi-organ virus SARS-CoV-2 can cast long shadows in many convalescents. Even after mild courses for those affected, persistent symptoms can remain in force for weeks and months, also designated as “Long-Covid” or “Post-Covid” syndrome. Extreme exhaustion (Post-Covid Fatigue), lethargy and pronounced fatigue, cognitive losses, lung and heart problems, persistent taste and smell disturbances as well as persistent pains (primarily in the chest) or an accelerated pulse are just some symptoms indicated for Long-Covid<sup>(2)</sup>.

A standardized definition of Post-Covid or Long-Covid does not yet exist. Some authors speak of chronic or Long-Covid syndrome when symptoms persist more than 3 months after the illness.

Acute Covid-19 infection lasts up to 4 weeks. Lengthy infections of 4-12 weeks are referred to as prolonged Covid-19 infections. Post-Covid syndrome (also known as PASC) can occur over 12 weeks. Nevertheless, the possibility of performing a PCR test is negative.

## Causes

The cause of the symptoms is not yet fully explained, most likely a reduced activity of the mitochondria is involved with it. The mitochondria are directly damaged by the Covid-19 virus, as well as by the proinflammatory cytokines during the acute infection. This may also explain why Post-Covid syndrome shows so many different images – from extreme fatigue, pain, depressive moods with tinnitus, shortness of breath in addition to gastrointestinal complaints. The symptoms coincide well with the known symptoms of mitochondriopathy.

## Ozone Therapy

The Paramed Center for Complementary Medicine is the leading institution in Switzerland for outpatient accompanying complementary therapy of Post-Covid syndromes. Since 2021 we offer corresponding outpatient consultation hours. Ozone therapy is an essential pillar of our widely diversified therapies for this indication.

In the context of an integrative therapy concept, patients are additionally treated with orthomolecular medicine, phytotherapy, mistletoe therapy and physical therapies. In our integrative setting, ozone therapy has always proven itself, particularly in the area of post-viral fatigue syndromes. These experiences could now also be implemented specifically for Post-Covid syndrome.

Ozone gas was discovered in 1840 by **Prof. Christian Friedrich Schönbein**, its chemical formula was determined in 1865<sup>(3)</sup>. The medical use of ozone (O<sub>3</sub>) was ultimately advanced by the scientists and inventors **Werner von Siemens** and **Nikola Tesla**, who developed the first ozone generators for medical purposes in the 19<sup>th</sup> century.

At the end of the 19<sup>th</sup> century ozone was used as a disinfectant, during the First World War also for wound disinfection<sup>(4)</sup>. In the 1920s experiments were carried out with ozone and hydrogen peroxide to treat influenza. In the interwar period and after the Second World War the use of medical ozone was widespread in Germany and other countries.

Ozone use became more widespread by the German physician **Wolff** who used it in his practice. In Europe there was then a merger of professional societies from Austria, Germany, Switzerland and Italy with the goal of creating standardized treatment guidelines<sup>(5)</sup>.

## Dosages

In therapeutic application different forms of treatment are distinguished. The so-called “large autologous blood treatment” [autohemotherapy] is the most common form of ozone therapy.

Usually 100-120 ml of blood together with 10 ml of sodium citrate are drawn into a 250 ml vacuum bottle. The range for safe blood collection volumes is 1.2-1.3 ml/kg of body weight. Depending on the type of ozone generator, up to 150 ml of O<sub>2</sub>/O<sub>3</sub> gas is then injected into the vacuum bottle either via a direct connection or via a syringe. After careful mixing the O<sub>3</sub> enriched blood is reinfused back into the patient.

With reference to the dosages of the ozone quantity added, it should be noted:

1. Low doses (10-15 µg/ml): These doses have an immunomodulatory effect and are used in situations where there is strong immunosuppression, e.g. cancer disease, senium, polymorbid conditions, post-viral fatigue, susceptibility to infections.
2. Medium doses (20-30 µg/ml): these have an immunomodulatory effect and stimulate the antioxidant protection system. They are very helpful in chronic degenerative diseases such as diabetes, arteriosclerosis, COPD, Parkinson, Alzheimer and senile dementia.
3. High doses (30-40 µg/ml): These have an inhibitory influence on autoimmune processes such as rheumatoid arthritis and lupus. Topically they are used especially for ulcers and infected wounds. Additionally they are used in the production of ozonated oils and ozonated water.

The European Society for Ozone Therapy has published a consensus paper concerning this with detailed explanations and an extensive collection of literature<sup>(6)</sup>.

Ozone concentrations of 10-15 µg/ml are recommended in the area of fatigue/exhaustion, which corresponds to an ozone quantity of 1000-2500 µg.

The optimal treatment sequence is 1-3 treatments per week.

The number of therapy sessions and the ozone dosage ultimately depends on the general condition of the person being treated, their age and any other underlying diseases.

As an applied general rule, the ozone dosage is adjusted in each case after 5 sessions.

Cycles of 6-10 treatments in each case are recommended in order to achieve an optimal effect. In the course of the treatment the patient's situation is once more assessed to determine other/further treatment cycles that perhaps are necessary. Clinical experience shows that the patient's condition improves markedly from about the 5<sup>th</sup> treatment session and the antioxidant protective mechanism noticeably improves after the 12<sup>th</sup> session.

If the redox balance (antioxidants/pro-oxidants) is unfavorable and the patient has an oxidative stress situation, a medium or high initial dose can lead to damage of the cellular antioxidant mechanisms and aggravate the clinical picture. Therefore it is highly recommended to start with low doses and then increase according to the patient's response.

During ozone therapy antioxidants such as Vitamin C and Vitamin E can be administered, and it should be noted that higher amounts of these substances in the blood interfere with the desired oxidative effect of ozone and thus weaken the effect of ozone therapy. Consequently oral substitutions with these vitamins should never take place during, but rather exclusively before or even better after ozone therapy. The relevance of this interaction depends on the bioavailability of the specific antioxidant. Any intravenous therapy to be given with antioxidants (e.g. Vitamin C, glutathione) should therefore not be carried out before or during, but rather exclusively after the administration of ozone. The optimal interval here amounts to half a day (e.g. Ozone therapy in the morning, taking the preparations in the evening).

It is important to get an idea of the patient's nutritional situation by means of anamnesis, or if necessary with the help of extended laboratory parameters. Nutrition as a source of exogenously supplied antioxidants plays an important role in the expected clinical response to ozone therapy.

### **Effect**

Experience shows that patients can be divided into 3 groups:

- Normo-responder
- Hyper-responder
- Hypo-responder

Basically the Arndt-Schultz Law also applies here (as with all regulatory procedures): weak stimuli fan, medium stimuli regulate, strong stimuli can block. This must absolutely be taken into account when adjusting ozone dosages over the course of the treatment series, which means that rigid treatment concepts with fixed dosing regimens should be rejected.

An important factor for the effect of ozone therapy is based on the hormesis principle: single or repeated exposure to a substance in low doses which is otherwise harmful increases the homeodynamics of a living system and thus the ability to self-regulate.

Experience also shows that within the scope of integrative application the overall performance of the mitochondria is improved. Healthy networked power-plants in the cells are an essential basis for functioning regulatory systems.

Since no receptors for ozone exist in the body, its mechanism of effect is understood as an indirect effect provided by mediators. In the area of treatment of post-viral functional disturbances, the effect is aimed at enzymes and mediators (cytokines) of cell metabolism. Specifically this is about:

- a) The body's own antioxidant protection systems with measurable increase of various antioxidant enzymes (superoxide dismutase, catalase, glutathione peroxidase, reductase)
- b) The immune system with release of endogenous cytokines such as interferon and interleukin
- c) The activation and suppression systems of gene regulation

Meanwhile on this basis a series of scientific studies on the effect: Tirelli et al. in a study with ME-/CFS patients in 2021 could establish a significant improvement in fatigue syndromes, without the occurrence of any relevant side effect<sup>(7)</sup>.

In a pilot study also in 2021 the group around *Adriana Schwartz*<sup>(8)</sup> could prove a tendential symptom improvement in 25 hospitalized patients with medium to severe Covid-19 symptoms, without any applied of side effects. Therefore a good treatment basis can be assumed without riskiness.

Morteza et al. conducted a literature search and came to the result that ozone therapy contains a high potential to modulate the immune response of patient within the context of Covid-19 infection when used early. Especially with Covid-19 pneumonia the goal would be to stop oxidative stress and ultimately the cytokine storm which could be possible with ozone therapy<sup>(9)</sup>.

Specifically on the question of application of ozone therapy, Tirelli et al. carried out a study in 2021 with 100 patients. All the patients had fallen ill with Covid-19 a maximum of 6 months before and everybody suffered from Post-Covid fatigue, which was assessed using the FSS Scoring System. 1-3 ozone therapies were carried out. 67% of patients showed improvements in regard to pain and fatigue regardless of gender and age<sup>(10)</sup>.

## **Compatibility**

In therapeutic everyday life in our practice with approx. 1,000 applications per year, ozone therapy is indicated as very well tolerated. Rarely observed is a short and temporary feeling of heat or a slight pain during ozone injection.

The use of ozone is contraindicated with:

- Glucose-6-phosphate dehydrogenase deficiency (favism, acute hemolytic anemia)
- Toxic hyperthyroidism, Graves' disease
- Thrombocytopenia of less than 50,000 Thc/ $\mu$ l
- Serious cardiovascular instability
- Acute alcohol intoxication
- Acute myocardial infarct
- Acute severe hemorrhage
- During an epileptic seizure
- Hemochromatosis
- Substitution therapy with copper or higher doses of iron

The latter two mentioned are relative contraindications but should be treated with caution due to the oxidative stress caused by ozone therapy, particularly what you want to avoid above all in

hemochromatosis. However depending on the “severity level” and the laboratory status ozone therapy can still be carried out. The situation is similar for iron and copper substitution – it is a question of dose: low doses of 30 mg of iron are not a problem while high doses of iron supplementation of 100 mg or iron infusions should not be carried out during ozone series if possible due to oxidation (or with an interval of 3-4 days).

### **Summary and Our Own Experiences**

In our Center ozone therapy is an indispensable part of the treatment spectrum for a variety of indications. Even in the case of chronic diseases and especially in the area of post-viral disorders there is a slowing down of the metabolism, accumulation of toxins, “metabolic waste” and over acidification of the body. This causes symptoms such as fatigue, immunodeficiency and susceptibility to disease. Ozone is also effective against pain as well as inflammatory processes and can be used against allergies. The feedback from our patients is very positive and a large portion regularly come for treatment series, also for the purpose of prevention.

For now the therapeutic dosage used in combination with individual orthomolecular substances is a promising treatment approach for Post-Covid syndrome. A case study should clarify our approach to it in daily practice.

### **Case Study**

A 45 year old female patient with a prehistory of asthmatic disorder fell ill out of complete health into Covid-19. The primary symptoms were runny nose, cough, body aches and sore throat as well as severely swollen lymph nodes in the cervical region. There was a fever up to 39.5°C. A prescription for ibuprofen 3 x 400 mg occurred through the family doctor: the patient was isolated at home for a total of 10 days. The symptoms slowly improved, but a pronounced fatigue described as “leaden” remained which was accompanied by the feeling of a “brain fog”. Her mnemonic performance was significantly reduced especially the ability to concentrate and short-term memory. This exhaustion, which was unusual for the patient which she had not experienced before, showed no further improvement in the next weeks.

A renewed visit to the family doctor furnished no new insights in the context of a physical examination and no special pathological findings could be determined in a basic laboratory diagnosis. Her “exhaustion” was mentioned as a diagnosis and there were no further therapeutic recommendations because everything was imperceptible.

However since the symptoms did not improve and thus the ability to work was massively impaired the patient introduced herself to my outpatient consultation. Based on the anamnesis the suspected diagnosis of “post-viral fatigue syndrome” could be made.

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In order to get to the bottom of possible causes, laboratory diagnostics were initiated. In addition to an examination of the blood count, the CRP and the liver values, the concentration of certain micronutrients in the blood was measured whereby deficiencies in the area of Vitamin D, Omega 3, B<sub>12</sub>, Q10 and carnitine were detected. Additionally a functional test of the mitochondria was initiated in the sense of a determination of the bioenergetic indexes<sup>(11)</sup> which showed a significantly reduced index of 1.6 (normal value >2). Through this diagnosis mitochondrial functional disturbance could be assumed to be central to the symptoms.

Mitochondropathy is often triggered by a viral infection as mitochondria are an essential component of the endogenous virus defence by protecting the intracellular virus recognition through the so-called MAVS (Mitochondrial Antiviral Signaling Protein) and then activating the innate/non-specific immune system. Even after healing of the viral infection, these functional disturbances remain and ultimately lead to an ATP deficit in the cells, which leads to a whole-body problem because practically all cells and/or organ systems are affected. This multi-system character also explains the polymorphic symptoms both in the physical as well as in the mental realms.

Based on the symptoms and the laboratory values collected an individual micronutrient therapy was put together and prescribed as an extemporaneous preparation. The micronutrients were taken with the aim of improving disturbed mitochondrial function and better mitogenesis, thus a new formation of non-functionally disturbed mitochondria. Additionally in parallel it was recommended the patient comply with a low-carb diet with a maximum daily amount of 120 g carbohydrate.

In order to positively influence her performance ability a little faster and above all to address the mental symptoms (brain fog) faster, the administration of 15 g galactose took place daily, divided into 3 daily portions. With the help of galactose which is metabolized independently of insulin, ATP can be produced faster and easier in the cells which compensates for the energy deficit.

However the central pillar of the therapy was ozone therapy with a dosage of 20 µg; this treatment was administered 2 times weekly.

With these measures the patient already showed first improvements after 3 weeks, above all concerning the feeling of exhaustion and drowsiness in the head. However physical performance ability was still significantly limited. This corresponds with expectations as mitochondrial therapy takes several weeks to achieve a perceptible effect.

Accordingly the therapy was continued unchanged – with orthomolecular medicine as the basis and accompanying ozone therapy. In a further treatment course 5-hydroxytryptophan (5-HTP) was taken orally to improve serotonin and melatonin production. Under this therapy regimen there was a steady improvement of symptoms. After a treatment period of 10 weeks the patient was almost symptom free.



### Conflict of Interest

The author states that there is no conflict of interest.

### The Author



**Dr. med. Simon Feldhaus** is a specialist in general medicine with certificates of competence in phytotherapy and interventional pain therapy, diplomas for Naturopathy and as a TCM Therapist. He heads the Department of Medical Services and is deputy of the Medical Management of the Outpatient Clinic at the Competence Centrum of Paramed AG in Baar and is president of SSAAMP.

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EHK 2022; 71:258-263

DOI 10.1055/a-1787-6442

ISSN 0014-0082

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Karl F. Haug Verlag in MVS Medizinverlage Stuttgart GmbH & Co.  
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