

# Micro-immunotherapy & Varicella zoster virus infections



### **Keep the virus in check**



#### List of abbreviations

APC Antigen presenting cells

DC Dendritic cells

**DNA** Deoxyribonucleic acid

CMV Cytomegaliovirus

CT Computed tomography

**EBV** Epstein-Barr virus

HIV Human Immunodeficiency Virus

HLA Human leukocyte antigen

HSV Herpes simplex virus

IFN Interferon

IFT Immunofluorescence test

Ig Immunglobulin

IL InterleukinLD Low doses

MRT Magnetic resonance tomography

NK cell Natural Killer cell

RNA Ribonucleic acid

**SNA** Specific nucleic acid

**SKP** Serial Kinetic Process

TH Helper cell

T8c Cytotoxic T8 cell

ULD Ultra-low doses

VZV Varicella zoster virus

## Immune support through micro-immunotherapy in VZV infections and associated conditions







#### **APPLICATION OF THE FORMULA ZONA**

\*According to the experience of doctors of the International Associations of Micro-immunotherapy



In acute infections



2-4 capsules / day until symptoms improve, then slowly reduce the dosage



Maintenance therapy



1 capsule / day for 3-6 months

#### **IMMUNOREGULATORY OBJECTIVES**



Prevent the proliferation of VZV and the infection of further cells



Support the immune response in VZV infection



Prevent associated diseases



When I started to work with micro-immunotherapy, I had a young patient (34 years old at the time) who had been complaining of partly severe, shooting, partly pressing pains in her left leg and foot for several weeks with varying intensity. These pains came with recurrent muscle fibrillations and pain on individual areas of the skin and the left leg.

There was no indication of a herpetic lesion either in the history or in the examination. Neither CT, MRI nor neurological examination provided any explanation. In addition, the patient was suffering from a severe histamine intolerance, severe food intolerances and IgE-mediated food allergies. Her professional and private situation was also difficult. In summary, it can be said that she was suffering from a rather profound exhaustion.

As I could not think of much more, I ordered various serologies and found massively elevated VZV IgG antibodies. Treatment with the micro-immunotherapy formula ZONA (initially 3 capsules/day with an interval of at least 2 hours between each intake) led to a noticeable reduction in leg complaints within 3 days. Fatigue and exhaustion also improved. The dosage was then reduced to 1 capsule/day and continued for almost 4 months.

For me, this was the first time that a zoster sine herpete, always described rather obliquely in the literature, could be diagnosed and well-treated.

#### **Testimonial**

#### Micro-immunotherapy & **VZV** infections



Dr Johanna Pfusterschmid (Vienna, Austria)

#### Introduction

The varicella zoster virus (VZV) belongs, like the herpes simplex virus (HSV) 1 and 2, the Epstein-Barr virus (EBV), or the cytomegalovirus (CMV), to the human herpesviruses that are found worldwide in the population and play a central role in the immune system of most people. Since these viruses have the ability to remain latent in the body after the initial infection and periodically reactivate, there is a lifelong interaction of the immune system with these "roommates".

The course of the infection depends significantly on the virus-host interaction. In most people, the infection is mild. However, in the case of an immature, weakened, or imbalanced immune system or when the virus attacks anatomical sites such as the central nervous system, the infection can lead to complications.

#### **VZV** infection: A brief overview

During primary infection, VZV attacks the skin and mucous membranes, manifesting as chickenpox. After primary infection, the virus remains latent in the ganglia of the cranial nerves and sensory spinal ganglia, entering a dormant phase where the infection is kept under control by the body's immune system. When the immune system is disrupted by physical or emotional stress, VZV reactivation can occur. The virus then travels along the affected nerve pathways, replicating in the ganglion and causing inflammation of the nerve tissue in the corresponding skin areas.

The reactivation of VZV can manifest in the form of shingles (Herpes Zoster). This acute phase is accompanied by visible efflorescences that are initially infectious and should therefore be treated accordingly.

Additionally, intense pain usually occurs in the affected skin segment and, depending on the case, also a general feeling of malaise (fatigue, tiredness). In some cases, affected patients may suffer from dermatome-dependent pain without accompanying skin changes (zoster sine herpete)<sup>1</sup>.

In immunocompetent patients, herpes zoster typically heals within two to four weeks. However, in cases of immunodeficiency, such as in cancer patients, HIV-infected patients, the elderly, or iatrogenically immunosuppressed patients, the risk of a chronic course of shingles increases.

As is well known, with advancing age, the intensity of pain increases in herpes zoster, which can persist for up to a month after the rash has subsided. If the pain persists for more than three months, post-herpetic neuralgia is present. In addition to neuropathic pain, dys- or paresthesia can also occur in the previously affected dermatome. Post-herpetic neuralgia presents a challenge for both the patient and the health professional in everyday practice.

Further possible complications are the ophthalmic herpes zoster and the otic herpes zoster.

#### **Diagnostic and therapeutic options**

In general, a visual diagnosis is possible for a VZV infection or reactivation. However, in case of uncertainty, serological tests or a PCR can be performed.

In uncomplicated chickenpox, treatment is usually purely symptomatic (e.g. topical dressings, anti-itch powders or lotions). In this way, the symptoms and accompanying effects can be alleviated while complications are prevented. For immunodeficient patients, specific antiviral treatment is also possible<sup>2</sup>.

In the case of herpes zoster, it is indicated to initiate antiviral therapy when the efflorescences appear acutely, in order to contain virus replication and thereby shorten the disease phase and counteract possible complications. The antiviral agent can be administered in combination with high doses of vitamin B12 or other B vitamins (to support nerve cells). Additional administration of painkillers is usually necessary. In any case, good therapeutic isolation of the affected area should be ensured to avoid generalisation of the zoster infection.

#### Role of the immune system in VZV infections

The immune system plays an important role in virus control during both primary infection and reactivation, as well as the latency phase of VZV.

The production of type I interferons (IFN- $\alpha$  and IFN- $\beta$ ), which exert an antiviral effect, represents an important mechanism of the innate immune response. In addition, NK cells are significantly involved in containing virus replication through the release of IFN- $\gamma$  as well as their cytotoxic activity<sup>3</sup>.

On the level of acquired immunity, T cells are of fundamental importance to keep VZV under control. CD4+ T cells contribute to the activation of cytotoxic CD8+ T cells responsible for lysing virus-infected cells through the release of interleukin 2 and IFN-y. In addition, T4 cells mediate the initiation of the humoral immune response with the production of VZV-specific antibodies. T and B memory cells formed within a few weeks after primary infection persist in the organism for a long time and are repeatedly boosted by reactivation or renewed exposure<sup>3</sup>.

However, VZV has developed numerous strategies to evade the immune response (immune evasion), such as downregulating interferon production. Moreover, VZV is capable of infecting immune cells such as dendritic cells and T cells, thereby impairing their functions<sup>4</sup>.



#### The micro-immunotherapy approach

Micro-immunotherapy, which draws on the natural functioning of the immune system, represents a valuable immunoregulatory treatment option in daily practice (Fig. 1). The treatment of choice for immune support in VZV infections or reactivations and associated conditions is the formula ZONA. The fields of application of this formula, which is composed of cytokines, ribonucleic acid (RNA), deoxyribonucleic acid (DNA) and specific nucleic acids in low doses (see Appendix 1), include chickenpox, herpes zoster and post-herpetic neuralgia.

The micro-immunotherapy formula ZONA is aimed at the following immunoregulatory objectives (see Appendix 1):

- Prevent the proliferation of VZV and the infection of further cells
- Support the immune response in VZV infection
- Prevent associated diseases

For acute VZV infections, 2-4 capsules / day are administered until symptoms improve, with a minimum interval of two hours between each intake. Depending on the case, it is recommended to continue the treatment with the formula at a maintenance dose of 1 capsule / day for a period of 3-6 months.

This treatment offers numerous benefits and is a particularly valuable support in everyday practice.

- The formula is not only aimed at virus control, but it also addresses underlying causal mechanisms such as existing immune dysfunctions, such as possible existing dysfunctions of the immune system, whereby the organism can be retrained to respond appropriately to internal and external stressors.
- Experience has shown that supporting the immune system in dealing with VZV usually leads to faster healing of lesions, relief of symptoms, and prevention of complications or sequelae such as post-zoster neuralgia.
- Micro-immunotherapy formulas are compatible with other treatment approaches and can be used in children, adults, and the elderly, as they have a good safety profile and are easy to take sublingually.

#### What is micro-immunotherapy?

Micro-immunotherapy is an immunotherapy in which immunomodulatory substances (mainly cytokines) are used in low doses to restore or maintain the balance of the immune system through targeted, sequential information transmission. This approach takes into account natural processes and ensures good tolerability (Fig. 1).





the chain of natural immune reactions, by following a specific sequential action.



RETRAINS

the immune system to respond appropriately to internal and external disruptive factors, thus resulting in long-term immune regulation.

Fig. 1: Mode of action of micro-immunotherapy

#### **Case reports**



#### Zoster sine herpete with eye pain

Dr Ina Chammah (Brunswick, Germany)

A 70-year-old patient visits my practice due to painful eyes, for which the ophthalmologist cannot find an explanation. She reports: "My eyes burn very often. The drops hardly help. In the evenings it is often very bad. In the right eye, I often feel like there is sand. The ophthalmologist says that I have to live with it. I can hardly bear the pain."

The mucous membranes in the nose, mouth, and vagina are moist. This almost rules out dryness of the eye due to a hormonal deficiency of estriol. Since I suspect a "zoster sine herpete," I arrange for a VZV serology, which provides evidence of reactivation of this herpes virus (elevated VZV IgG and IgA antibodies).

Subsequently, I initiate the following treatment:

- Formula ZONA (1 capsule / day for 2 months) (Immune support in VZV infections or reactivations)
- Formula EID (1 capsule / day for 2 months) (Non-specific immune support)

After 10 days, the patient reports an improvement in symptoms. The treatment with micro-immunotherapy formulas continues unchanged and the following vital substances are also administered:

- Sublingual vitamin B12 (5000  $\mu g/day$ ) and folic acid (400 m g/day) for 4 weeks (nerve-calming and antiviral supportive therapy)
- Lysine (3000 mg/day for 10 days and then 1g/day for 4 months) (nerve-calming and antiviral supportive therapy)

After another 15 days, the patient reports that she is pain-free and no longer needs eye drops. I recommend that the patient continue the treatment. After 2 months, the treatment with the micro-immunotherapy formulas ZONA and EID is administered at a maintenance dose of 1 capsule / day for 10 consecutive days each month for another 3 months.



#### Practical tip

In cases of neuralgic pain without a clear cause, it is advisable to rule out VZV reactivation diagnostically and to treat it accordingly if there is a corresponding burden. This usually alleviates or completely resolves symptoms and positively affects the clinical condition of the patients.

#### P

#### Practical tip

The formula ZONA can be synergistically combined with the formula EID and other treatment approaches, such as micronutrient therapy or microbiological therapy.



# Post-herpetic neuralgia Dr Petra Blum (Tegernsee, Germany)

A 66-year-old patient who owns a gourmet restaurant visits my practice due to severe pain. He reports an acute case of shingles a few months ago, which had spread from the 11th thoracic vertebra to the 4th lumbar vertebra, as well as in the left and anterior thoracic area down to the navel. He was treated with antiviral medication and a zinc paste. Since then, he has had unbearable pain that can only be somewhat controlled with a high dose of pain medication. The pain has increased in intensity, and he cannot sleep, finding it difficult to lie down due to the pain.

He has always been fit and healthy. The restaurant is now only open on weekends, as it requires a lot of effort and energy from him. During the examination, the healed areas of the herpes zoster are clearly noticeable

So far, he has been treated with the following medication:

- Aciclovir (5 x 800 mg/day)
- Ibuprofen (4 x 600 mg/day)
- Novalgin (4 x 40 drops/day)
- Tilidin (4 x 600 mg/day)

Since then, he says, he has had a sensitive stomach and high blood pressure (up to 200 mmHg systolic).

I set up the following treatment plan:

- Micro-immunotherapy formula ZONA (3 x 1 capsule / day) (Immune support for VZV infections or reactivations)
- Micro-immunotherapy formula INFLAM (1 x 1 capsule / day) (Dampen inflammation and alleviate pain)
- B-vitamins, Coenzyme Q10 (100 mg / day) (Nerve-calming and antiviral supportive therapy)
- Vitamin C (2 g / day) (Nerve-calming and antiviral supportive therapy)
- Lysine (1500 mg / day) (Nerve-calming and antiviral supportive therapy)
- Internal healing clay (2 x 1 teaspoon / day) (Stomach protection)
- Aconit pain oil (apply multiple times a day) (Pain relief)

At the same time, the previous medication is maintained, but the intake of Aciclovir is reduced to 3 x 800 mg/day.

Since the patient lives over 200 km away, the discussion of the further course of treatment takes place over the phone.

5 days later, the intake of Tilidin and Ibuprofen is reduced to 3 x 600 mg/day and Aciclovir to 2 x 800 mg/day, as there is an improvement in symptoms. The remaining treatment remains unchanged.

10 days later, Tilidin and Aciclovir are discontinued as the pain is no longer felt as intensely. The intake of Ibuprofen is reduced to 2 x 600 mg/day and Novalgin to 3 x 40 drops/day. The remaining treatment continues unchanged.

17 days later, the improvement in the patient's symptoms persists. The same treatment is maintained, but the intake of the formula ZONA is reduced to 2 x 1 capsules / day.

30 days later, the patient comes to my practice and he is feeling much better. The pain has decreased and his sleep is restful. The stomach problems have improved. He reopens the restaurant 6 days a week.

The examination shows a pallor of the skin and a decrease in touch sensitivity.

The following treatment is prescribed:

- Ibuprofen (1 x 600 mg/day)
- Novalgin (2 x 30 drops/day)
- Micro-immunotherapy formula ZONA (2 x 1 capsules / day)
- Micro-immunotherapy formula EID (2 x 1 capsules / day) (general immune support)
- B vitamins, Coenzyme Q10 (100 mg/day)
- Vitamin C (1 g/day)
- Internal healing clay (1 x 1 teaspoon/day)

Furthermore, osteopathy is prescribed to release adhesions.

44 days later, the patient calls and informs me that he has now stopped all painkillers. He is working full-time again and feels productive.

The following treatment was prescribed for the patient for the next 3 months:

- Methylcobalamin/Adenosylcobalamin (7 drops/day)
- Micro-immunotherapy formula ZONA (2 x 1 capsule/day for 2 weeks and then 1 x 1 capsule/day)
- Micro-immunotherapy formula EID (1 x 1 capsule/day)
- Vitamin C (1000 mg/day)

At the last check-up, the patient was feeling well and was very grateful that he could resume his normal daily routine.



The formula ZONA can be easily used in daily practice by assessing the patient's clinical symptoms and laboratory findings. In more complex cases, it may be helpful to perform a lymphocyte typing to determine the immune status. In cases of non-adaptation with lymphopenia/hyporeactivity, the formula ZONA can be combined with the formula EID for 4-6 months or longer if necessary. In cases of non-adaptation with lymphocytosis/hyperreactivity, the formula ZONA is combined with the formula EAI for 1-2 months and then for an additional 2-4 months.

#### **Conclusion**

Micro-immunotherapy is a valuable and safe treatment option for VZV infections or reactivations and associated conditions that can be prescribed in both children and adults in daily practice. Experience has shown that by supporting the immune system, there is usually a faster healing of the lesions, relief of symptoms and prevention of complications or sequelae such as post-herpetic neuralgia.



## Annex 1: Immunoregulatory objectives of the micro-immunotherapy formula ZONA

The micro-immunotherapy formula ZONA is composed of a specific combination of immunomodulatory substances in low doses (LD) & ultra-low doses (ULD). This formula, which is used in VZV infections or reactivations and associated clinical pictures, aims to have an effect on the overall system with multiple objectives (Fig. 2 & 3).

The mechanism of action of the formula ZONA is described in more detail below.

#### Viral cell cycle of VZV

- Prevent VZV replication and infection of further cells
- The specific nucleic acid SNA®ZONA in ULD is directed against VZV.
- The use of interferon alpha (IFN-a) in ULD is aimed at maintaining the biological activity of this cytokine, thus protecting uninfected cells from VZV infection and preventing the virus from spreading from cell to cell.

The active ingredients contained in the micro-immunotherapy formulas are processed according to a specific preparation mode called "Serial Kinetic Process" (SKP). It consists of a 1:100 serial dilution process, followed by a vertical shaking. These steps undergo a predetermined number of repetitions. Depending on the preparation, the effect of the substances may vary<sup>5-8</sup>.

The active ingredients used in LD aim to upregulate the activity of the substance in the organism according to its natural physiological effect (shown in green in Fig. 2). In contrast, the substances used in ULD are designed to modulate or maintain (shown in blue) or downregulate (shown in red) the activity of the substance in the organism <sup>8-11</sup>.

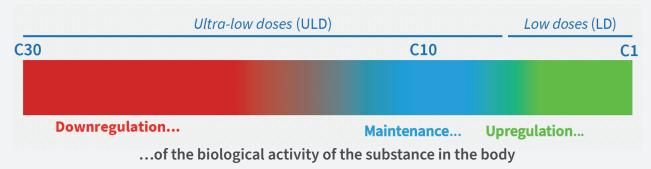


Fig. 2: Objectives of the active ingredients contained in the micro-immunotherapy formulas depending on their preparation mode.

There is an extensive literature that describes the reversal of the effect of immunomodulatory substances and other stimuli, depending on the applied dosage. This phenomenon is called hormesis and refers to an adaptive response that is triggered by weak stimuli in the organism to optimize its functioning and resistance to greater stress<sup>9-10</sup>. This biological phenomenon of hormesis could provide an explanation for the functioning of LD & ULD used in micro-immunotherapy<sup>5-8</sup>.

#### The immune response to VZV

- Support the immune response in VZV infections
- The use of ribonucleic acid (RNA) and deoxyribonucleic acid (DNA) in ULD is aimed at activating mature dendritic cells (DC) and inititating the THI response without overstimulating it.
- The use of interleukin 2 (IL-2) in ULD is aimed at maintaining the biological activity of this cytokine, which supports the functions of NK cells, T-helper cells (TH), and cytotoxic T8 cells (T8c) that play an important role in fighting virus-infected cells.

#### **VZV-associated conditions**

- Prevent associated diseases
- The use of SNA®-HLA I in ULD is aimed at downregulating the expression of HLA I molecules to favour the lysis of virus-infected cells by NK cells.
- The use of SNA®-HLA II in ULD is aimed at downregulating the expression of HLA-DR molecules in non-professional antigen presenting cells (APCs) to counteract uncontrolled inflammatory processes and associated diseases.

Link to the complete description of the Model of the mechanism of action of the formula **ZONA** 



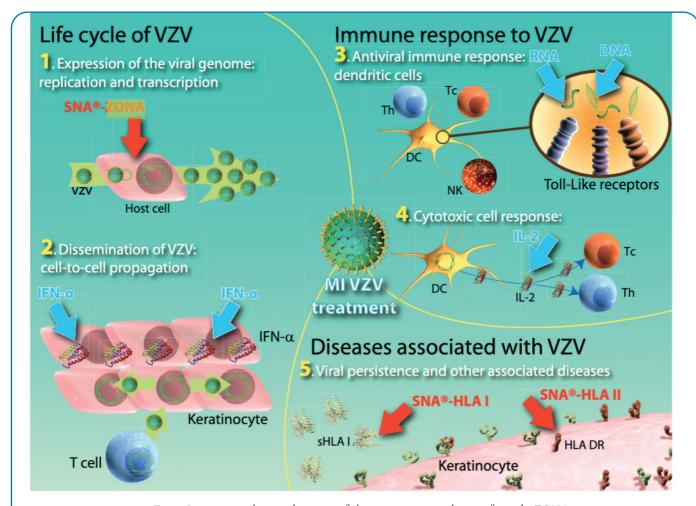


Fig. 3: Immunoregulatory objectives of the micro-immunotherapy formula ZONA

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