

Micro-immunotherapy & Urinary Tract Infections



This brochure is for doctors and other health professionals only



Summary

Urinary tract infections (UTIs) are an increasingly frequent reason for consultation in clinical practice. They are often treated with antibiotics, which can not only lead to increased antimicrobial resistance, but can also impair the immune system, our protective shield against pathogens. The interface between the innate and the adaptive immune system is the pacesetter for the further course of the infection. Micro-immunotherapy acts precisely at this level in order to help the immune system regain its natural efficiency in defending the organism against infections through targeted transmission of information.

The Immune System: Our Shield Against Infections

The number of urinary tract infections has been steadily increasing in recent years, with 80% of cases caused by uropathogenic E. coli (UPEC)¹. However, our body is equipped with a powerful ally, the immune system, which acts as the organism's protective shield against pathogens. In urinary tract infections, it is important to fight the pathogens as quickly as possible while avoiding excessive damage to the urothelium as a result of the inflammatory processes. The further course of the infection depends largely on immune balance^{2,3}.

However, treatment with antibiotics mostly contrib-

utes to a weakening of our highly complex natural defence system, reducing the learning effect on immunological memory. Nonetheless, it is of course important to prevent complications such as pyelonephritis.

In the case of infections of all kinds, micro-immunotherapy (low-dose immunotherapy), which draws from the natural functioning of the immune system, provides a valuable immunoregulatory tool in clinical practice to balance the immune response and promote its efficacy in urinary tract infections.

The Immune Response In Urinary Tract Infections

Structural (including the urothelium) and biochemical barriers (acid pH and urine transport) provide the first line of defence against uropathogens. In addition, various soluble factors (including uromodulin, antimicrobial peptides, pentraxins and secretory IgA) exert a protective effect. In addition to their function as a protective barrier, epithelial cells are able to recognise pathogens such as bacteria via specific toll-like receptors and to initiate the innate immune response via cytokines such as interleukin 1 (IL-1), interleukin 6 (IL-6) and interleukin 8 (IL-8).

Numerous immune cells are present in the urinary tract. Resident macrophages play an important role in the defence against pathogens, releasing proinflammatory cytokines such as interleukin 1 (IL-1), as well as tumour necrosis factor alpha (TNF-a) and chemokines, which activate or recruit other immune cells to the site of infection. Besides macrophages, mast cells are also found in the submucosa. In the early phase of the infection, these cells tend to have a proinflammatory effect through the secretion of histamine and TNF-a, among others, although as the infection progresses they increasingly exert an antiinflammatory or immunosuppressive effect through the release of interleukin 10 (IL-10).

Among the cells that are recruited from the blood, neutrophil granulocytes are particularly noteworthy, as they are fundamental for the elimination of bacteria, mainly via phagocytosis. In contrast to the innate immune response, the responsiveness of adaptive immunity in the urinary tract - especially in the bladder - is rather limited. This dysfunction is thought to be due to the production of IL-10 by mast cells, which resolves the immunoinflammatory response prematurely to avoid possible damage to the uroepithelium. This prevents effective elimination of bacteria, whereby the risk of recurrent infections increases^{2,3}.



Treatment of Urinary Tract Infections

In UTIs, the usual therapeutic measures are mainly based on the administration of antibiotics. However, in patients who require continuous or even prophylactic antibiotic therapy, these treatments eventually lose their efficacy, contribute to the deterioration of the normal flora, facilitating the increase of resistance and, above all, do not prevent recurrences.

In this sense, there is an increasing need for immunomodulatory treatments that help to strengthen the immune response in UTIs and that can be combined with antibiotic treatment, if needed, and other treatment approaches in a strategy at different levels.

Through the use of immune mediators in low doses, micro-immunotherapy communicates with the immune system in its own language with the aim of training it back to a balanced and effective response (Fig.1). It can be combined with other treatment approaches and is suitable for all age groups.



Fig. 1.: Summary of the mode of action of micro-immunotherapy formulas.

As part of an integrated therapeutic strategy in UTIs, micro-immunotherapy's immunoregulatory action can be combined with other measures aimed at the following objectives:

- **Reimplant beneficial bacteria** and promote a microenvironment that supports vaginal and urethral health: oral or vaginal probiotics (Lactobacillus Crispatus, Iners, Jensenii and Gasseri)
- Hinder the adhesion of uropathogenic bacteria to the uroepithelium: cranberry, D-Mannose or Juniper.
- Combat bacteria that cause UTIs: essential oils (oregano) they should be EOs that respect beneficial intestinal bacteria and eliminate opportunistic pathogens such as enterobacteria, skin bacteria, or yeasts.
- Prevent opportunistic bacteria from adhering to the mucosa: optimal hydration (internal and external), sitz baths with intimate gel respectful of the microbiota and vaginal pH and a few drops of tea tree essential oil.



The Micro-immunotherapy Approach

Micro-immunotherapy, or low-dose immunotherapy, uses immunomodulatory substances (mainly cytokines) in low doses to restore or maintain the balance of the immune system through **targeted and sequential transmission of information.** As an immunomodulatory therapy, micro-immunotherapy is of interest in urinary tract infections to support the immune response. It can be used with the following objectives:



The **formula EID** is the micro-immunotherapy formula used for all types of infections. It is particularly suitable for recurrent infections and can also be used to accompany antibiotic treatment. It is aimed at the following immunoregulatory objectives:

- Support innate and adaptive immunity and thus provide general immune support.
- Counteract mechanisms that alter or inactivate the antimicrobial defense while at the same time preventing immune overactivation.
- Increase phagocytic activity and promote the release of proinflammatory cytokines by favoring the Th1 response.



The Micro-Immunotherapy Formula EID Exhibits an Immunostimulant Effect by Boosting Both Innate and Adaptive Immune Responses



Experience has shown that the use of this formula can reduce the need for antibiotics in many banal infections - including urinary tract infections - without any complications typical of infections.



According to the clinical experience of doctors of the international micro-immunotherapy associations (AEMI, IFMi, MeGeMIT). It is important to establish a therapeutic strategy on the basis of the patient's clinic, determining priorities in each individual case in order to ensure adherence to treatment.

NOTE: In case of persistent and/or recurrent infections, it may be advisable to resort to specific laboratory tests such as lymphocyte typing (cellular immune status) or protein profiling (humoral immune status) in order to better assess the state of the immune system and adjust the micro-immunotherapy treatment accordingly. Herpesviruses - especially the Epstein-Barr virus (EBV) as well as the cytomegalovirus (CMV) - should be checked serologically (preferably via immunofluorescence tests). It is known that these herpesviruses have an immunosuppressive effect via released virokines and, according to experience, are often a significant contributing factor to recurrent infections - also in the urinary tract.

If an active infection or reactivation of these viruses is detected, antiviral micro-immunotherapy formulas such as the formula EBV (immune support in EBV infections or reactivations) or the formula CMV (immune support in CMV infections or reactivations) can be used in combination

Control and reduce inflammation and its mediators, in patients with intense pain associated with the infection.

To modulate inflammation in patients who suffer from intense pain associated with a urinary tract infection, the micro-immunotherapy **formula ARTH** can be used. It is aimed at the following immunoregulatory objectives:

- Specifically regulate the overexpression of inflammatory mediators such as interleukin 1 (IL-1) and tumour necrosis factor alpha (TNF-α)
- Counteract tissue dysfunction, halt structural damage and loss of function.
- Favour the resolution of inflammation and prevent chronification.



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Counteract the inflammatory and immunosuppressive effects promoted by stress and anxiety, often linked to recurrences of these infections, and the fear of new infections.

The formula MISEN can be used in UTIs with the following immunoregulatory objectives:

- Prevent immune depletion and exhaustion associated with stress and senescence, promoting immune defence and helping to prevent associated diseases such as infections.
- Prevent accelerated ageing favoured by psychological distress.
- Modulate the decrease in telomerase and favour cell regeneration.
- Balance glucocorticoid levels, acting upon the cortisol/DHEA ratio, whilst compensating for the inflammatory effects linked to cortisol increase.



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We when is the use of the formula EID-N preferred over EID and vice versa?

Both the formula EID and EID-N are aimed at exerting an immunostimulatory effect and providing general immune support in acute, chronic and recurrent infections. Although both formulas support cellular immunity, the formula EID-N promotes the TH1 pathway more strongly and thus has a greater proinflammatory effect than the formula EID, which is specifically directed at maintaining balance between cellular and humoral immunity whilst promoting mucosal immunity. Hence, the use of either formula will depend on the general immune status of the patient and the criteria of the health professional. In patients with autoimmune diseases or an autoinflammatory background, the use of the formula EID is generally preferred, whereas the formula EID-N is recommended for patients with cellular immunodeficiency, TH1/TH2 disequilibria and associated recurrent infections.

Can the formula EID be combined with the formula ARTH / INFLAM?

The formula ARTH and the formula EID have opposite immunoregulatory objectives (anti-inflammatory and immunostimulatory, respectively), whereby using them together is not usually recommended. However, in patients suffering from intense pain due to excessive inflammation, an alternate treatment regime with the formulas EID and ARTH can be applied so as to stimulate the immune response while normalising inflammatory pathways. In these cases, it is important to observe the following treatment regime: the immunostimulatory formula EID should be taken in the morning, as a general immune support, and the formula ARTH at night, a minimum of 12 hours apart, to reduce inflammation without interfering with the action of the formula EID.

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Clinical Benefit Of Micro-immunotherapy In UTIs



It is of interest to reduce infectious episodes and other impactful **treatments in patients with recurrent infec-tions.**

Conclusion

Micro-immunotherapy is a valuable therapeutic tool in numerous clinical pictures and has proven beneficial as a general immune support in infections of all kinds. It is aimed at strengthening the defence mechanisms in a gentle and targeted way to enhance their action against pathogens. As part of a multilevel

Reference

- 1. Song J, Abraham SN. Innate and adaptive immune responses in the urinary tract. Eur J Clin Invest. 2008 Oct;38 Suppl 2:21-8.
- 2. Ortega Martell JA. Immunology of urinary tract infections. GMS Infect Dis. 2020;8:Doc21
- 3. Abraham SN, Miao Y. The nature of immune responses to urinary tract infections. Nat Rev Immunol. 2015;15(10):655-663.

treatment strategy in UTIs, it contributes to bringing the infection under control and preventing recurrences by restoring an efficient immune function, thus benefiting the patient's long-term health and reducing the need for antibiotic treatment.

4. Jacques C, Chatelais M, Fekir K, Fauconnier L, Mellier M, Togbe D, Floris I. The Micro-Immunotherapy Medicine 2LEID Exhibits an Immunostimulant Effect by Boosting Both Innate and Adaptive Immune Responses. International Journal of Molecular Sciences. 2022; 23(1):110.





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