urexent®

Patient information

Autologous immunotherapy for the causal treatment of atopic diseases like neurodermatitis and allergic rhinitis in children and adolescents

Content

01 | Background on atopic diseases

Atopic diseases such as neurodermatitis and allergic rhinitis cause hypersensitivity reactions of the immune system to external influences. At present, it is not possible to cure these diseases, therefore the therapy is usually symptomatic. Unlike other treatment methods, the drug urexent® targets the cause of the disease directly. The drug, which is based on the patient's own bodily substances, has an immunomodulating effect and is easy to use as an oral drop preparation.

Observations from practice have shown for a long time that atopic diseases frequently occur within the family. Today it is known that people affected form increased evels of IgE antibodies and that the number of granulocytes used for parasite defence is increased (eosinophils). As a result, the immune system reacts to normally non-immunogenic substances. This is also evident from a measurable imbalance in the activity of T helper cells: The response of type 2 T helper cells dominates.[1, 2, 3] These trigger the activation of B lymphocytes, eosinophils and mast cells. The B lymphocytes secrete IgE that targets harmless substances; mast cells and eosinophils release inflammatory histamine or ECP (Eosinophil Cationic Protein); this results in inflammation, which is accompanied by redness and itching as well as tissue damage due to scratching.

The immune system goes crazy

Environmental influences play a major role in atopic diseases, but stress situations can also lead to a relapsing course. Both factors have a considerable influence on the immune system. And this is already happening in early childhood: When the maternal antibodies, which the infant has at its disposal for several months due to placental transfer, are depleted, the immune system faces for the first time the task of independently distinguishing the body's own structures from foreign ones and assessing whether an immune response is necessary. In 40% of children, the immune system reacts inappropriately to non-immunogenic substances in the form of an allergic reaction. About a quarter of all children suffer from neurodermatitis.[1]

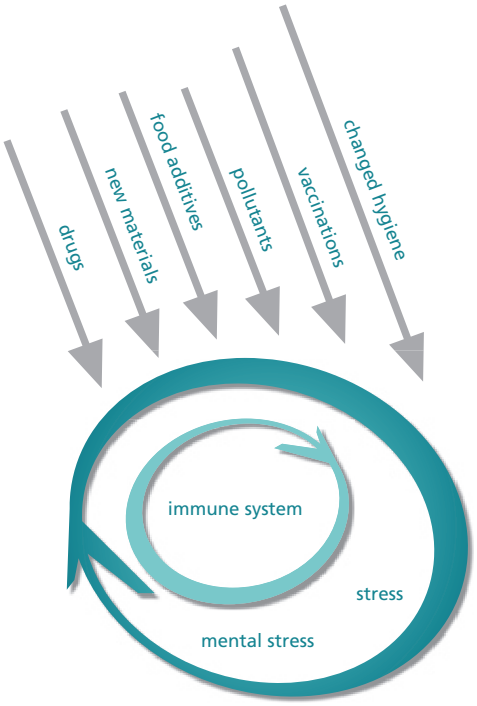

Figure 1: Influences on the immune system

02 | Approaches to causal treatment

Disease patterns that become noticeable owing to clear external signs are treated almost exclusively symptomatically, especially if the pathophysiological connections are not completely clarified. This often also applies to the treatment of atopic diseases. Ointments and creams are used to restore the skin barrier in the case of neurodermatitis. In worse cases, glucocorticoids are used, which are also used for allergic asthma. However, this does not eliminate the cause of the diseases, which means that treatment is not usually successful over the long term and some significant side effects occur.

A causal therapy modulates the imbalanced immune system. Autologous immunotherapy with the urexent® preparation is based on the patient's own urine and can normalise the activity of T helper cells. This reduces or prevents an excessive reaction by the immune system, as occurs in neurodermatitis or allergic rhinitis, and provides long-lasting relief of symptoms or even freedom from symptoms[5].

03 | urexent® – therapeutic success and mode of action

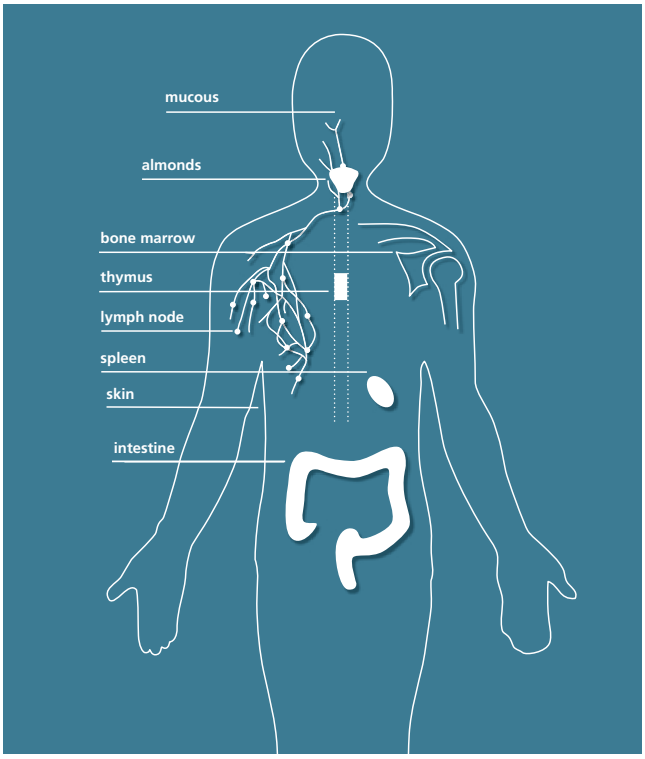

Figure 2: The human immune system

Individual medicine - targeted and tolerated

Since atopic diseases are based on a malfunction of the immune system, urexent® is suitable for the treatment of these diseases due to its immunomodulating mode of action. Since the immune system is just as individual as the person it is supposed to protect against diseases, an autologous therapy is the most appropriate treatment for the patient. This is especially true for toddlers and teenagers, where the immune system is often confronted with specific challenges.

In general, urexent® is extremely well tolerated due to the use of the patient's own bodily substances, is almost free of side effects and therefore also suitable for newborns and breastfeeding infants. The drug is manufactured in a controlled environment according to pharmaceutical standards subject to the guidelines of the Medicinal Products Act and the AMWHV (Decree for the Manufacture of Medicinal Products and Active Pharmaceutical Ingredients). The drug is produced in accordance with the strictest hygiene requirements, thus guaranteeing a high-quality drug that is manufactured specifically for each patient.

Results of urexent® treatment on patients with neurodermatitis

The effectiveness of urexent® can be demonstrated not only by the appearance of patients treated with it. After the first six treatment months, 73% of the patients showed a significant improvement in their health. After completion of the 12-month therapy, 85% of the patients were able to achieve a sustained full or partial remission. [4] These treatment results can be demonstrated over a period of four years – observations of long-term success are currently being carried out.

However, the immunomodulating effect is particularly remarkable: urexent® can restore the balance between the immune response of the type 1 and type T helper cells. 5 This is shown by the interleukin-2 and interferon-γ levels, which are regulated by the type 1 cells. The therapy causes an increase in the level of both cytokines, which in atopic patients decreases by 6 or 7 times, and at the same time reduces the IgE and ECP concentration by half. [5]

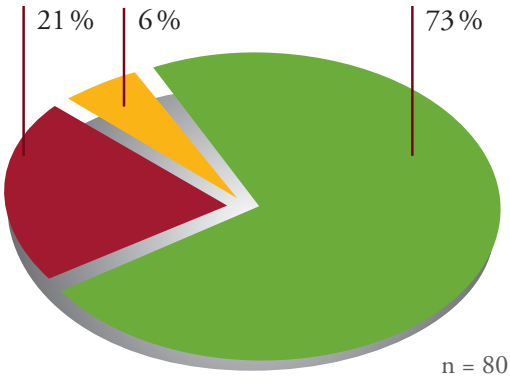

Figure 3: Treatment success in patients suffering from neurodermatitis approx. 6 months after starting urexent® therapy

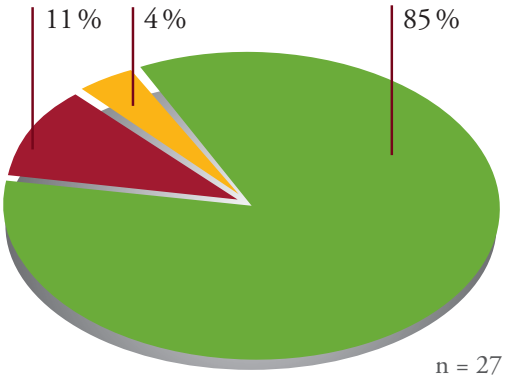

Figure 4: State of health of patients suffering from neurodermatitis up to 4 years after completion of urexent® therapy

improved unchanged worsened

The mode of action in detail*

The immunomodulating effect is based on a substance that is often initially perceived as harmful - ozone. It is regarded as a trigger for oxidative stress[6]. But like in many other cases: The dose makes the poison. In the case of neurodermatitis, it is known that oxidative stress in the skin is measurably increased during acute phases.[1] An ozone therapy therefore does not seem to be beneficial. However, it is known that the immune system itself produces ozone - as part of normal physiological reactions - in order, for example, to kill bacteria via the chemical properties of ozone that cause cell wall damage. [7,8]

Recent studies show that trioxygen induces the formation of antioxidative enzymes by means of the second messenger principle and thus counteracts strong oxidative stress.[6] This is done via transcription factors that act on more than 230 different genes. In addition to enzymatic activation, this gene regulation could also restore the balance between the two types of T helper cells.

In autologous immunotherapy with urexent®, ozone is used to oxidise acute phase proteins derived from the body's own substance - urine. In addition to the second messenger effect described above, the immune system

substances contained in urine, in particular IgA and IgG, could regulate the excessive concentration of IgE in the patient and at the same time promote the response of the type 1 T helper cells via IL-2. In addition, the oxidised proteins also act as antigens in the body, triggering an anti-antibody reaction (network theory by Niels Jerne from 1974, Nobel Prize for Medicine 1984), causing the immune system to recognise IgE that is targeting harmless antigens (allergens).

urexent® is absorbed as an oral drop preparation through the mouth and throat mucosa. There, the oxidatively modified proteins cause the formation of antioxidative enzymes, which then reach their site of action via the extensive lymphatic system. As with some naturopathic preparations, urexent® can in rare cases lead to an initial aggravation, which usually disappears after a short time and can be regulated by adjusting the dosage.

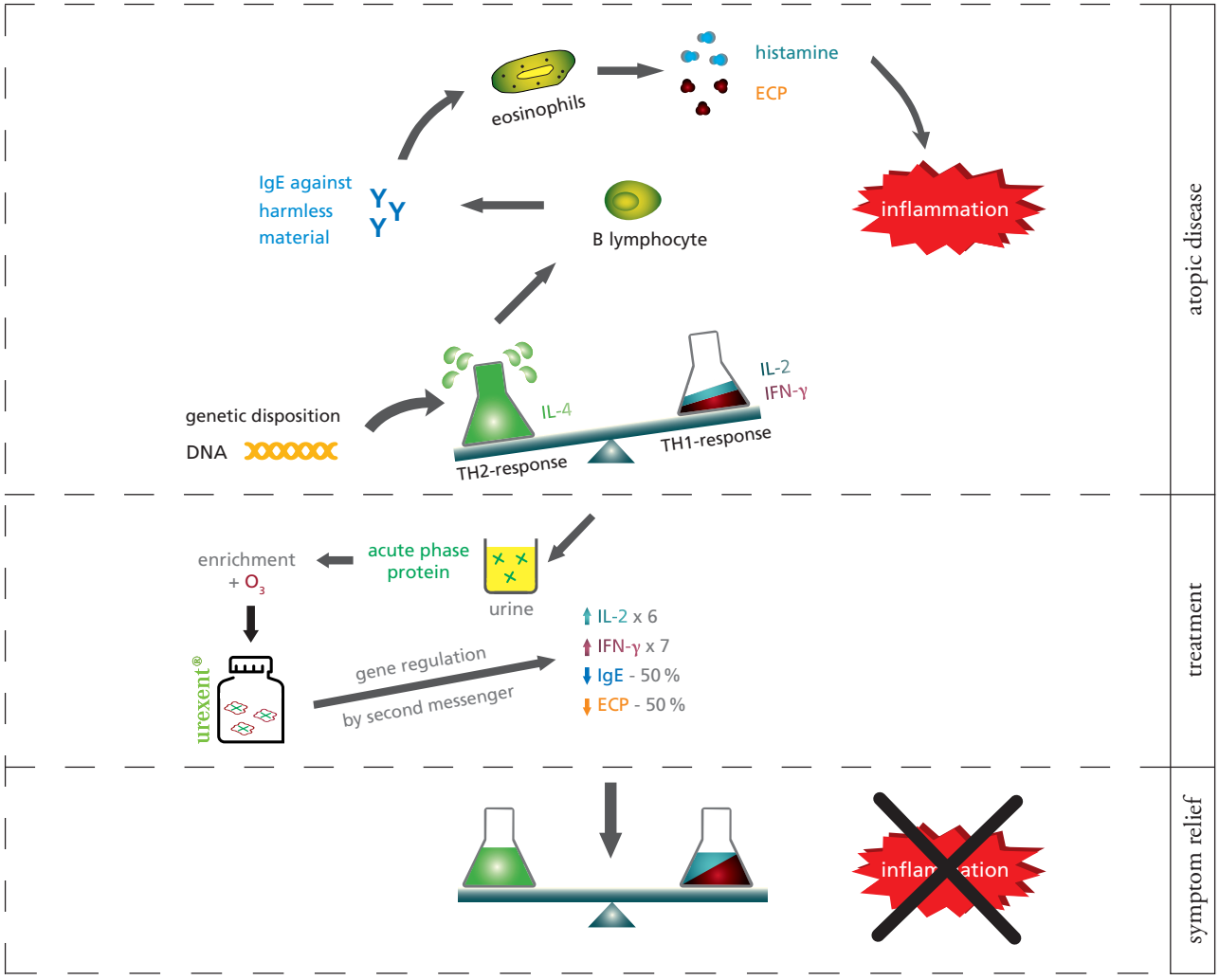

Figure 5: Possible mechanism of action of urexent®

04 | urexent® in practice

urexent® can currently be prescribed to the patient using a "grünes Rezept" (green prescription for over-the-counter drugs). If the patient opts for the treatment, the therapist can request all necessary documents and materials from FBM-PHARMA, which organises and coordinates the entire procedure. After the patient has provided his/her urine sample in the practice, it is collected by a specialised logistician and taken to the FBM-PHARMA production facility. Following the qualitative microbiological control of the incoming goods, standardised pharmaceutical production takes place in the clean rooms, followed by the final product control and the validated release for placing the product on the market by the responsible parties. In order to offer both the patient and the therapist the best possible service, the drug is delivered to the patient's local pharmacy after approximately two to three weeks. Thanks to this full service, the therapist is able to concentrate entirely on the care of the patient.

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[1] Ji H, Li XK: Oxidative Stress in Atopic Dermatitis. In: Oxid Med Cell Longev.2016; 2016:2721469.doi:10.1155/2016/2721469. Epub 2016 Feb 23.

[2] Kapp A.: The role of eosinophilic granulocytes for the pathogenesis of atopic dermatitis /neurodermatitis. Eosinophilic products as markers of disease activity. In: Hautarzt. 1993 Jul;44(7):432-6.

[3] Czarnowicki T, et al.: Early pediatric atopic dermatitis shows only a cutaneous lymphocyte antigen (CLA)(+) TH2/TH1 cell imbalance, whereas adults acquire CLA(+) TH22/TC22 cell subsets. In: J Allergy Clin Immunol. 2015 Oct;136(4):941-951.e3. doi: 10.1016/j.jaci.2015.05.049. Epub 2015 Aug 1

[4] Eigene Erhebung durch FBM-PHARMA.

[5] FBM-PHARMA, data on file (Messungen durchgeführt an der Uni Heidelberg, mittels ELISA-Test).

[6] Zanardi I, Borrelli E, Valacchi G, Travagli V, Bocci V.: Ozone: A Multifaceted Molecule with Unexpected Therapeutic Activity. In: Curr Med Chem. 2016;23(4):304-14.

[7] Babior BM, Takeuchi C, Ruedi J, Gutierrez A, Wentworth P Jr.: Investigating antibody-catalyzed ozone generation by human neutrophils. In: Proc Natl Acad Sci U S A. 2003 Mar 18;100(6):3031-4. Epub 2003 Feb 24.

[8] Wentworth P Jr., et al.: Evidence for Antibody-Catalyzed Ozone Formation in Bacterial Killing and Inflammation. In: Science. 13 Dec 2002:Vol. 298, Issue 5601, pp. 2195-2199,DOI: 10.1126/science.1077642.

* The mechanisms and modes of action described in this document are derived mechanisms based on the findings of scientific literature and empirical medicine.

If you have any questions, the FBM-PHARMA GmbH team, as a specialist in individual immunotherapy, will be happy to assist you or put you in contact with an FBM-PHARMA GmbH-affiliated therapist.

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